

Hermaphroditos
THE HUMAN INTERSEX

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BY

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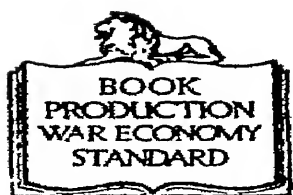


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PREFACE TO THE SECOND EDITION

THE object of this work has been the isolation of groups of intersexes possessing common clinical features and arising from particular physiopathological disturbances, *i.e.*, from particular modes of malfunction of the mechanism of sex determination.

For this reason I have studied first the physiopathology of intersexuality. To orient myself in the maze of experimental research towards a synthetic conception useful for clinical work, I followed not only the natural historical approach but also the cultural historical approach, which I believe to be a necessary complement to the natural historical method.

This double approach led to certain conclusions developed in the first edition and as yet unchallenged. These are the Hellenic conception of the existence of only two classes of intersex, male and female, and the non-existence of "true" hermaphrodites; consideration of intersexuality as of a normal phenomenon; study of the condition according to the degree of intersexualisation as shown by biological experiments; the importance of mild intersexualities; and the constitutional, not exclusively endocrinological, approach to the therapeutic problem.

In this edition I have re-written the chapter on the physiopathology of intersexuality so as to make clearer the existence of two great physiopathological classes of intersexuality, the deep constitutional and the endocrine intersexualities—a distinction important from both the clinical and the therapeutic stand-points. I have also re-written the clinical chapters so as to clarify the various forms in which intersexuality manifests itself to the clinician.

Notwithstanding the remarks in certain reviews of the first edition I have not added more references, because my object has not been to quote all the work done on this subject but to extract general principles from the many publications on the biological basis of intersexuality. Neither have I added any illustrations of my own cases, as I do not feel justified in bringing before the public eye patients who came to me for advice. The method, adopted by many authors, of publishing such photographs with a mask distracts from the most important morphological element, the facies. I have therefore maintained the classical figures of intersexes which have already been published.

A. P. CAWADIAS.

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INTRODUCTION

THIS book constitutes the development of my Thomas Vicary Lecture on Hermaphroditism. I take this opportunity of expressing my gratitude to Sir Hugh Lett, under whose presidency of the Royal College of Surgeons I was chosen to give this lecture, and to the present President, Sir Alfred Webb-Johnson, who occupied the chair when I gave the lecture. In developing in this lecture the biological ideas on the human intersex inspired by the work of John Hunter, the patron saint of the Royal College of Surgeons, I had also before me the inspiration of the name of Thomas Vicary, one of the sixteenth-century giants with the intuition of a great humane and scientific healing art.

* * *

The human intersex presents one of the most fascinating problems of constitutional medicine, and the interest it has always aroused is reflected in the enormous literature on the subject. Despite this voluminous work, however, clinical and physiopathological views evince so much vagueness that definite lines of therapeutic action are lacking. This is because our knowledge of the subject is extremely disconnected. Collections of cases, even when observed thoroughly, and reports of individual experiments, do not of themselves constitute science, which, as Plato says, is "only of the general" and thus consists of leading principles. I have had the opportunity of studying many intersexes, as they amount to a great proportion of the practice of an internist interested in endocrine and constitutional states. I have read much of the massive literature on the subject. But I do not intend to give extracts from my case-books nor yet a compilation of my reading. My object is to reflect on my cases and those of others in order to discover directive lines of clinical action.

This necessitates a synthetic view possible only through the method of historical thinking, which in medicine consists in considering an actual medical problem in the light of all that has led up to it. Historical thinking is thus based on historical knowledge, which becomes Benedetto Croce's "most perfect form of knowledge." It is based on the real history of medicine,

which is not an outline of medical periods, study of the lives of physicians of the past nor the reading of old texts—all this is only a preparation for history—but knowledge of the development of work and (ideas on particular medical problems.) The fullest understanding of a medical situation, and consequently the most effective action, are the result of this historical thinking. Thus history of medicine is in the last resort reflection for action. It is not a theoretical occupation for dilettantes and littérateurs but a necessity for the research worker and the practising clinician.

Next to historical thinking, it is biological thinking that clarifies most effectively the problem of the intersex. We are living in one of the most brilliant periods of medicine, the biological period. We view man and all living beings not as a bundle of organs or a colony of cells but as an integrated whole. The unit in biology, and thus in scientific medicine, is the living being, the organism as a whole, the body-mind in its particular environment, not the cell or organ. Instead of studying organs and functions analytically we study total biological reactions. Instead of endeavouring to explain the functions of the body-mind in terms of physics or chemistry we centre our conceptions in life itself as an independent phenomenon. This biological principle, the guide of the ancient Greek physicians, re-introduced into medicine by John Hunter and later by Charles Darwin, and developed more recently by physiologists of the whole man such as Gaskell, Sherrington and J. B. S. Haldane, finds its application in the work of contemporary physicians.

This biological principle, which in clinical terminology becomes constitutional principle, guides our study of intersexuality. Historical as well as biological thinking will reveal to us two classes of human intersex, male and female, and show the so-called complete or true hermaphrodite to be a speculative construction derived from the dæmonology of old. Furthermore, biological thinking leads us to study the intersex not as a fictional morbid category to be classified in the glass cases of a pathological museum in its various genera, families and species, but as a type of psychophysical human structure, a constitutional type, a biotype. In the light of experimental biology the human intersex shows many gradations and shades. Contrary to the view perceptible in older works on intersexuality, it is the mild intersexes which are the more interesting, while the very rare monstrous intersexes, the so-called pseudo-hermaphrodites and hermaphro-

dites of our fathers, are useful principally for the understanding they afford of the extremely frequent milder forms. It is in fact to these milder intersexual states that I seek to draw the attention of my colleagues. They are by far the most common, and knowledge of them has great practical consequences. This knowledge enables us to understand much of the behaviour, psychology and reaction to disease of a great number of our patients. for ultimately intersexuality is an element in the understanding of the individual patient, a part of diagnosis of the person. Thus its clinical application is very extensive.

CHAPTER I

DEFINITION AND GENERAL CONCEPTION OF INTERSEXUALITY

INTERSEXUALITY is a condition of imperfect sexual differentiation. A male intersex is an imperfect male, in other words, a feminised male. A female intersex is an imperfect female, a masculinised female. Thus the intersex is an individual in whom male and female features co-exist in varying proportions.

Hermaphroditism in olden days meant bisexuality. As bisexuality never exists in humans it can be considered to-day as synonymous with intersexuality, as a poetical expression of intersexuality. From a more precise nosographical point of view the term hermaphroditism is applied to severe intersexes, *i.e.*, those genetic males in whom feminisation bears on the genital organs and gonads, and those genetic females in whom masculinisation bears on the same structures.

Intersexuality is a normal condition in humans. There is no perfect male nor perfect female, but all males have certain rudimentary female features and *vice versa*. Accentuation of this normal condition constitutes clinical or morbid intersexuality. There are thus several degrees of intersexualisation, several gradations between the "fruste" intersexualities so frequently encountered in medical practice and the monstrous hermaphrodites which delighted the teratological and naturalistic interests of our fathers.

This morbid intersexuality represents a constitutional disturbance, *i.e.*, one involving particularly the system of integration of the body, the system regulating the constitution, the psychophysical construction, the biochemistry or metabolism of the individual. The system is composed of the psychoassociational cortex or psyche (the summit of integration), the genes and organisers, the neurovisceral or vegetative system, the neuro-metabolic or endocrine system, and environmental, mainly nutritive, factors.

The Two Classes of Intersex, the Male or Androgynoid, the Female or Gynandroid. Since the days of the ancient Greek physicians who first studied the human intersex scientifically, two classes of such

individuals are distinguished according to the predominant sex, male or female. Male intersexes are men who show in their psychophysical structure many female features, female intersexes are women with male features in their psychophysical make-up. Male intersexes can be termed androgynoids, the Greek expression for "men looking like women" (a term not to be confused with androgyne, which designates a man-woman), and female intersexes can be designated gynandroids. Our textbooks still contain the terms "male pseudo-hermaphrodite" and "female pseudo-hermaphrodite," which are inadequate and should be jettisoned. Hermaphroditism is or is not. There are no false diseases, but only false diagnoses. Facts are never false, but only the interpretation placed on them. Far greater clarity in clinical work will be obtained if we maintain the simple division of the ancient Greeks and deal with the subject in terms of male and female intersexes (androgynoids and gynandroids) whatever the degree of intersexuality.

The Non-existent Third Class of Human Intersex, "True" or Complete Hermaphroditism, Androgynism: A Comedy of Errors. For many centuries study of the human intersex has been marred by the intrusion of demonology and ancient Eastern superstition into scientific work. Mystical notions have maintained the possibility of a third class of intersex, the bisexual individuals or "complete hermaphrodites," whom Klebs with dogmatic self-sufficiency has called "true" hermaphrodites.

This conception, crystallised even to-day in our textbooks, originated in the legends of the ancient Eastern (or pre-Hellenic) peoples. To explain the two sexes of human beings these peoples believed that the first humans were bisexual "androgynoi" who divided later, one-half giving rise to males, the other to females. This legend is retold by Plato in his Symposium. The primitive Adam also seems, according to some old theologians, to have been an androgyne or hermaphrodite who separated later into the definite male Adam and the female Eve. Further, to symbolise fertility the races of the ancient East believed in the existence of bisexual deities. The Greeks, who added to their Aryan religion of the twelve Olympian gods many of the ancient Oriental deities, took a bisexual divinity to whom they gave the name Hermaphroditos (the son of Hermes and Aphrodite). With them, however, the bisexual was only a minor deity, and more of an artistic poetical creation than an article of faith.

As physicians, however, the Greeks remained unhampered by old legends or religious speculation. Accurate observers and free from superstition, they saw men who looked like women and women who resembled men, but never human beings who were man and woman at the same time, never human replicas of the Hermaphrodites of their sculptors. They accepted two classes of intersex, the male and the female, and rejected in human biology the existence of androgynes or bisexual beings.

The Romans, however, had neither the accurate powers of observation nor the strict scientific reasoning of the Greeks. They were swayed by legend and superstition, and introduced into human biology the conception of bisexual humans. The naïve Pliny set the ball rolling. He writes of the existence of androgynoi and introduces the term hermaphrodite applied to humans. He was led to this not only by the old legends but also by the fairy tales of travellers in which they boasted of wonders seen in distant lands. It was from travellers that he heard of the Androgynoi, "men who unite both sexes in the same individual and perform alternatively the functions of each," who live in a country situated "above that of the Nasomones and the Machylae." Such fantastic flights, originating in biologists whose powers of observation were poor, are responsible for the introduction into medicine of the concept of human bisexuals, thus linking human biology with the ancient Eastern dæmonology from which the Greeks had temporarily freed the human intellect.

Dæmonology dies hard, and once installed in medicine the concept of complete hermaphroditism became generally accepted. The Renaissance physicians and ~~those of the seventeenth and eighteenth centuries~~ maintained it on the basis of flimsy arguments. Ambroise Paré believed in bisexual humans because there exist individuals whose sexual behaviour is alternatively male and female. Arnaud offered as a demonstration of complete human hermaphroditism the tale of two hermaphrodites of Valencia who married each other, each becoming pregnant through mutual ministrations. And the fantasy does not end there. Affaitatus Fortunius accepts the "fact" of self-fertilisation, and tells us that the magician Merlin was the product of a self-fertilised hermaphrodite. *Ignotus per ignotum.*

None of these arguments could resist even an elementary scientific criticism, and the conception of true hermaphroditism was tottering in the nineteenth century when certain anatomo-

clinicians such as Klebs stepped into the breach and tried to save it by the anatomical argument. According to Klebs, whose work is repeated parrot-like in all our textbooks, complete hermaphrodites exist because there are individuals with both testes and ovaries. So dense are the anatomical blinkers of this distinguished pupil of Virchow that he writes, "It is unimportant whether in these individuals the ovarian or testicular element is rudimentary and not functioning," and in fact in nearly all cases of "true hermaphroditism" either the female or the male glandular element is rudimentary. But rudimentary testicular tissue is found in practically all women, and all men, according to some histologists, show female glandular cells, and moreover all men secrete the female hormone oestrin. Thus the anatomical argument explodes spontaneously through *reductio ad absurdum*.

The final stroke against the conception of true or complete hermaphroditism was given by modern biological work. In the first place, sex has been demonstrated as based not in the gonads but in the genes, the gonads being important executives. A male is not male because he has testes; he has testes because he is a male, and similarly a female is a female not because she has ovaries but has ovaries because she is a female. Experimentation has shown that genetic males can be feminised to such a degree as to have their gonads partially feminised, the result being an animal with testis and ovaries. Similar intersexualisation of the gonads can be obtained by masculinising a genetically female animal, the result again being an animal with testis and ovary. Therefore when a human being possesses gonads of both sexes, he does not call for ~~notation of a bisexualism~~ such as that of ~~certain lower animals~~. ¹ Humans possessing both testis and ovary are either genetic males or genetic females in whom intersexualisation has progressed far.

It is time therefore to remove from our textbooks the chapter on complete or true hermaphroditism, which we have seen to be merely a remnant of ancient dæmonology introduced into medicine purely on speculative grounds, maintained for centuries by the most fantastic and flimsy of arguments, but shown to be completely erroneous by modern biological work.

Only in certain lower living beings is true hermaphroditism seen. But these are double animals consisting of a male and a female united. They result sexually from the parallel development of both a masculinising and a feminising sex-formative

impulse.¹ Animals in which the sexes have separated (gonochorists) can never be hermaphrodites. It is a contradiction in terms.

Intersexuality as a Normal Phenomenon, Morbid Intersexuality as Exaggeration of a Normal Process. Charles Darwin was the first to point out that intersexuality is a normal phenomenon. There is no absolute male nor absolute female. Every male possesses latent female features, and *vice versa*. Thus the so-called "normal" male and female represent the lowest degree of intersexuality, which is thus a physiological phenomenon. Clinical intersexualism, intersexual states with which physicians are called upon to deal, represent therefore an exaggeration of a normal process, all degrees being found between the "normal" (which is a latent intersex) and monstrous hermaphrodites. *Natura in operationibus suis non fecit saltus*. Intersexuality, like many other diseases, is made in us, by us, for us.

Progression from the "normal" intersex to the most severe forms of pathological intersexuality is demonstrated in experimental work and clinical observation. R. Goldschmidt has done an enormous amount of experimental work on the subject, his brilliant researches being marred only by unwarranted speculative conclusions. R. K. Burns, R. R. Humphrey, Kozelka and Gallagher, C. A. Pfeiffer, F. R. Lillie are other representative names. Their experiments show that according to the intensity of the masculinising process applied in a genetically female embryo, and to its conditions of receptivity, various degrees of intersexualisation (*i.e.*, masculinisation of the female animal) can be obtained. When the masculinising process is weak, masculinisation bears only on certain extra-genital characters. With a stronger masculinising process the external genitals and the genital tract are masculinised, as in Pfeiffer's experiments. With an even stronger masculinising process the female gonads are partially masculinised and the animal possesses testis as well as ovaries, as shown in experiments on parabiosis and grafts in amphibians (Burns, Humphrey), after injections of male hormones into hen eggs (Gallagher and co-workers), and in some instances of freemartin. In very intense masculinisation both the female gonads are transformed into testes, as in the freemartin and some of the experiments on parabiosis in amphibians. A similar

¹ In the first edition I described this impulse as "sexoformic," from *sexus* and *forma*. Although this is a good Latin construction, I have adopted the term "sex-formative" in order to avoid any confusion, however far-fetched, with ~~sexum~~ and ~~formica~~.

gradation is seen in the experimental feminisation of genetically male embryos. Thus we pass progressively from intersexualisation of the extra-genital characters to involvement of the genital organs and tract, and then to partial intersexualisation of the gonads, finally to complete intersexualisation of both gonads constituting complete sex reversal.

Similar gradation is apparent in the clinical observations of intersexes. The first group comprises individuals in whom the extra-genital characters are intersexualised. In a second group the genital organs and tract are affected. A more advanced stage is represented by cases in which the gonads themselves are partially intersexualised, the patient possessing ovary and testis. Whether in human pathology we reach the stage at which intersexualism involves the whole gonadal tissue, a genetic male possessing only ovaries and a genetic female possessing only testes, we do not know.

Comparison between clinical and experimental gradation is one more argument against true or complete hermaphroditism. Experimentally genetic males can be intersexualised to the point of possessing ovary and testis, genetic females to the corresponding stage. Thus the "true" hermaphrodites of our textbooks are simply males or females who have attained this high degree of intersexuality, which, we gather from experimental work, does not represent even the highest degree of intersexualisation.

CHAPTER II

PHYSIOLOGY OF SEX FORMATION

INTERSEXUALITY consists in imperfect sex differentiation or sex formation. Humans and most animals are gonochorists, i.e., living beings who are separated into male and female individuals, and in them a definite mechanism causes each individual to become male or female. When this sex-forming mechanism is disturbed the result is an intersex. The physiopathology of intersexuality is thus bound up with sex formation.

Sex, for ancient Greek physicians, was centred in the gonads. A male was a male because he had testes. Aretaios wrote that semen maketh man, and Virchow resumed this train of thought, which persisted up to the end of the nineteenth century, in the aphorism *propter ovarium mulier est quod est*. At the end of the nineteenth century biologists and clinicians enthroned sex in the endocrines. A male was a male because his endocrines, including the testis, were such as to secrete a preponderance of masculinising sexual hormones, and a female was a female for analogous reasons. Biedl, modifying Virchow's aphorism, wrote *propter glandulas endocrinas mulier est quod est*. Contemporary opinion centres sex in the genes. A male is a male because in the fertilised ovum which represents the first stage of his development masculinising genes preponderate over the feminising.

The genic masculinising or feminising function is carried out by two groups of executives, the organisers of which little is known, and the endocrines including the gonads. The endocrines thus become the executives of the genic sex-formative impulse, continuing and perfecting masculinisation or feminisation and maintaining the sex-differential features throughout life. In this view the gonads descend from their ruling position in sex formation to that of important executives. A male is not a male because he has a testis, but he has testis because he is a male, and similarly woman is not the appendage of her ovaries but has ovaries because she is a woman. Instances of humans without gonads but possessing definite sexual characters have been described (Halban, Robert Meyer and others).

THE SYSTEM OF SEX DETERMINATION

The system of sex determination, the mechanism which causes an animal to be male or female, consists in an interaction of (a) a biological field or field of individuation, (b) a sex-formative impulse, (c) a biological environment.

The Biological Field. The conception of the biological field, derived from that of the magnetic field, developed mainly through the work of Joseph Needham and Charles Waddington. It is penetrating very slowly into medical thought because we are accustomed to think in terms of material localisation, not in terms of dynamics, of lines of force. However, a dynamic description of the events of animal development, as well as of all biological events, is undoubtedly an enormous improvement upon static descriptions of anatomy. The concept of biological field is a powerful aid in codifying the order of development of man's formation.

The term biological field denotes in terms of energetics a morphological and pre-morphological domain actively organising itself (Waddington). Thus it represents in terms of energetics one aspect of the developing living being, the fertilised ovum, the unicellular organism, as well as the embryonic mass. It is not a simple geometrical symbol. It is a real entity, a system of forces which can be isolated in the living being.

The conception of the biological field arose out of the following facts. Speemann has shown that if at a very early stage of embryonic development a piece of the dorsal lip of the blastopore is taken and grafted on to another embryo, in the blastula or early gastrula stage this piece (the central organiser) will induce the neighbouring host to form a secondary embryo, often including nerve, tube, brain, eye, somites, notochord. But in the determination of the main axis of the new, the induced embryo, two processes must be distinguished, (1) determination that an embryonic axis will be developed, (2) determination of the character of that axis, i.e., that one end shall be head, another tail. The former process is termed evocation, the latter individuation. In a transplantation the evocation is always performed by the graft, the organiser; the individuation seems always to be carried out by graft and host working together. Evocation is hormonal in character; individuation (a modern translation of the old "reactivity") requires a new conception, the biological

field. In other words, there interact in the developing animal two systems of forces, composed respectively of the organising impulse and the field. Both have the power of self-determination.

From the point of view of sexual development, the biological field of the human embryo is bisexual. It has potentialities for the development of male and female characters, and if imagined theoretically to be abandoned to its power of self-determination the result would be a mixture of male and female characters without plan or harmony in the embryo. This bisexual potentiality is transmitted by heredity, for, as Charles Darwin noted, the living being is a product of male and female and thus has the latent features of both.

On the basis of the self-determination and bisexual potentialities of the field, certain male and female rudiments develop during the bisexual or sexually undifferentiated phase of the human embryo. Johannes Wier, the famous sixteenth-century physician, had the intuition of embryonic bisexuality, which in terms of modern embryology is field bisexuality. On this field the organising sex-formative impulse, part of the general organising impulse in embryonic development, acts. The organising impulse is always unisexual. A masculinising sex-formative impulse stimulates through various executives the development of male potentialities within the field and inhibits that of female potentialities, the contrary occurring for a feminising impulse.

The Sex-formative Impulse. This impulse acts on the field and organises it as a male or female animal. In humans it is always unisexual, stimulating the male potentialities of the field and inhibiting the female or conversely. It arises in the genes and acts through two groups of executives, the sex organisers and the sex endocrines.

The Sex Genes. The sex-formative impulse is initiated in the sex genes. These are included in X and Y chromosomes, and act as ferment producers or endocrines on the rest of the cell. Each ovum possesses one X chromosome. Sperm may possess either an X or a Y chromosome. The X chromosomes possess feminising genes, the Y chromosomes masculinising genes. The fertilised ovum resulting from the union of an X ovum and an X sperm shows a predominantly feminising genic balance. In other words, it initiates a feminising sex-formative impulse. The fertilised ovum resulting from union of an X ovum and a Y sperm shows a predominantly masculinising genic balance, and initiates a

masculinising impulse. When the masculinising genes found in the Y chromosome or the feminising genes found in the X chromosome are not sufficiently powerful, the resulting gene combination or balance is abnormal and intersexuality follows. This insufficiency of sex genes, Goldschmidt believes, may be hereditary or result from a spontaneous gene mutation.

The sex genes are the nuclear controllers of sex. They control only the cell, through a ferment acting on the cell alone. As they are transmitted to all cells of the body deriving from the division of the fertilised ovum, through interaction with field forces a masculinising or feminising character is imparted to each cell and thus to all organs deriving from the association of these cells. In certain insects, for example in *Drosophilæ*, the genes are the sole sex-organising element. In higher beings, however, complexity of morphogenesis has led to development of two other kinds of control, the sex organisers and the sex endocrines.

The Sex Organisers. The general organising impulse originating in the genes organises the embryonic mass by determining the differentiation of certain minute organs of endocrine secretion, the "organisers." These specialise in secreting certain morphogenetic hormones of sterol type (thus akin to adult sexual hormones and growth vitamin D) by means of which the amorphous embryonic mass is "organised," i.e., arranged in particular parts or organs. As all parts and organs have a specific sexual stamp, male or female, the organisers contribute to this stamp, and thus are in part sex organisers. These primitive morphogenetic endocrines masculinise or feminise all parts and organs, but also they determine differentiation of the gonads and definite endocrines which, as a third series of controls, continue and perfect masculinisation or feminisation. In the description of the biological field Speemann's original experiment, through which the concept of organisers was introduced into medicine, was delineated. The endocrine nature of the organisers and the chemical determination of probably their chief hormone has been elucidated by J. Needham and C. Waddington. As in the genes, a masculinising or feminising impulse is generated in the sex organisers according to the masculinising or feminising predominance in their hormone secretions. The sex-regulating function of the organisers centres in their secretions which, unlike the genes, act not only on one cell but on various adjacent cells, although only in the immediate neighbourhood.

The Sex Endocrines. The sex endocrines, particularly the gonads, constitute the third group of executives of the sex-formative impulse. They are thus instruments of that impulse, and not the basis of sex formation. Halban was the first to stress this point, on the ground that humans can show definite sexual characters, male or female, in spite of complete absence of gonads (observations of Rössell and Wallau, Robert Meyer). Furthermore, certain sexual characters, *e.g.*, the male plumage of fowls, do not depend on the gonads or other sex endocrines, as demonstrated by the fact that they are not influenced by castration.

With these reserves it can safely be said, however, that the endocrine element of the sex-formative impulse has received the most complete demonstration, clinical and experimental. This is due to greater ease of research, and thus does not justify the exclusively endocrinological view of sex formation at which many physicians still linger. Even our conception of the endocrines has been modified of recent years, as I have described in a paper on the "History of Endocrinology." They can no longer be considered separately from the other regulators of metabolism, the genes and organisers; and they are connected with the nervous system, constituting in fact the terminal effectors of that part of the nervous system through which metabolism is regulated.

The endocrines and particularly the gonads, acting independently or under the influence of the nervous system, secrete masculinising or feminising hormones through which the sex-formative impulse continues and develops in embryonic and post-embryonic life. The masculinising hormones are testosterone from the testis, corticosterone and possibly other androgens from the adrenal cortex, and progesterone from the ovaries which, however, has become adapted to other functions not concerned with sex formation. Feminising hormones are the ovarian oestrogens, antepituitary prolactin and possibly, in part, thyroxine. Both groups of hormones are found in all humans, male as well as female; and in the last resort it is predominance of one or the other group that makes for masculinisation or feminisation. Sex is ultimately a matter of balance—balance of hormones, of organiser inductor secretions and of sex genes.

The sex-regulating action of the endocrines is exerted not on one cell alone as in the case of the genes, nor on the cells of the immediate neighbourhood as in that of the organisers, but on all

cells of the body. The development of the endocrines makes for a more diffuse and thus a more general metabolic action

The Terminal Points of Attack of the Sex-formative Impulse. The sex-formative impulse invades ultimately the various parts and organs of the body, including the central nervous system and the psycho-associational cortex. All parts and organs are masculinised or feminised by the ferments elaborated in the genes and acting exclusively on the cell containing these genes, by the internal secretions or "inductors" of the sex organisers acting on cell groups or organs but requiring some degree of direct contact, and by the internal secretions of the endocrines or hormones acting more diffusely on cell groups and organs.

Thus in the sex-formative mechanism four phases can be distinguished: (a) the genetic phase, (b) the organiser phase, (c) the endocrine phase, (d) the organ phase.

The Biological Environment. The rôle of environment in the smooth running of the sex-formative mechanism is shown by the disturbances in sex formation which are evident after changes in the environment. This has been demonstrated through experiments bearing on lower animals, of which a few examples follow.

The oldest experiment is that of Giard (1886), who showed that when male crabs are parasitised by other crustaceans such as *Peltogaster* they develop the external characters of the female. Even the testis of the crab may degenerate. Thus the parasite, by setting up metabolic disturbances in its host, by modifying the internal or humoral environment, disturbs the normal sex-formative mechanism.

Richard Hertwig has shown that by affecting the environment so as to delay fertilisation of frog's eggs, the proportion of males is greatly increased, and in extreme cases all the eggs produce males. In other words, the balance of the genes may be overriden by environmental factors, and testes may develop in a frog whose internal chromosomal balance would have resulted in an initial feminising impulse.

Extensive investigation in various laboratories show that in larval amphibians extremely low temperatures retard the medullary development of the gonad and direct the animal towards the female sex. The contrary occurs with extremely high temperatures. In warm-blooded animals the reverse sensitivity has been observed.

The action of environmental factors on the endocrine phase of

sex formation has been demonstrated extensively, not only in animals but up to a certain point in man. Disease of the gonads and other sex-formative endocrines affects sex differentiation. The sex-formative endocrines are susceptible to factors of nutrition (under-nourishment, lack of certain vitamins such as E).

Finally, in man there is also a social, educational and psychological environment to be considered as affecting the sex-formative mechanism. An individual, for example, may have a genetic masculinising impulse giving rise to masculinising organisers and these in turn to masculinising endocrines, but educational environmental factors may interfere and the individual become homosexual, i.e., in part a male intersexual.

DEVELOPMENT OF THE SEXUAL CHARACTERS

The interaction of sex-formative impulse, biological field and biological environment causes the developing animal to become male or female ; in other words, it endows the animal with male or female sexual characters.

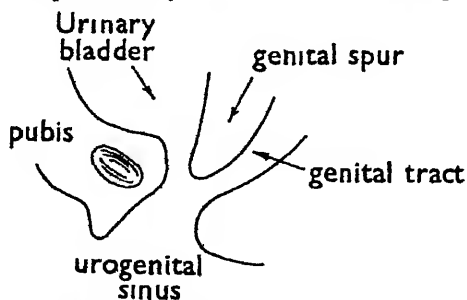
The development of these characters follows a definite pattern. (a) At the start of development the animal is asexual ; (b) next comes a phase of bisexuality determined by the self-differentiation of the "field," in which rudiments of male and female characters are found : (c) last comes the phase of unisexuality (which, as already said, is never absolute). Through the action of the sex-formative impulse on the "field," rudimentary sexual features belonging to one sex develop and those of the other are inhibited. Thus these organs and tissues acquire a definite unisexual stamp and the whole animal becomes male or female.

The gonad is seen only in the 5-7 mm. embryo, and thus before this the animal is in the asexual stage. When first detected the gonad is bisexual, both male and female cells being found, and this bisexuality lasts up to the seventh week. The female cells constituting Pflüger's cords localise in the cortex of the gland, the male cells in the medulla. The gland is thus an ovotestis. Under the influence of a masculinising impulse transmitted through the sex genes and the sex organisers, the cortical female formation of the gonad is inhibited and atrophies, and the medullary male portion develops. The contrary occurs when the sex-formative impulse is feminising. Thus the stage of unisexuality is reached.

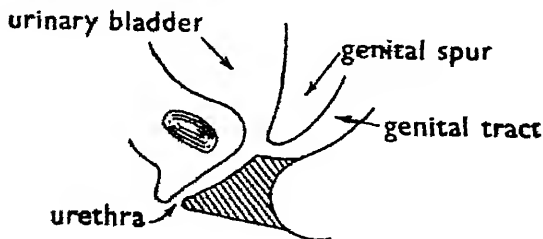
The genital tract, appearing after the asexual phase of em-

bryonic development, is represented by the gonoducts. In the bisexual stage two pairs of ducts exist, the Wolffian or male ducts, and the Müllerian or female ducts. Under the influence of the masculinising sex-formative impulse transmitted through the internal secretion of the sex-formative organisers, or that of the male gonad already developed, the female Müllerian tract disappears, leaving as its only traces the vestigial formations of appendix testis, utricula and verumontanum. The male Wolffian duct develops into the vasa deferentia with its inferior diverticula, the seminal vesicles. Under the influence of a feminising sex-formative impulse, transmitted in the same manner as the masculinising impulse, the male Wolffian ducts disappear, leaving as vestiges the paroophoron and Gärtner's canal. The female Müllerian ducts develop and in their superior portion constitute the tubes, in their inferior portion uniting to form uterus and vagina.

The urogenital sinus is also bisexual in its early phase. The gonoducts open at this early bisexual phase into a perineal cavity, the urogenital sinus, which receives also the urinary tract. The two tracts are separated by the formation called genital spur.



Under the influence of a masculinising sex-formative impulse transmitted through organisers and testis, the urinary tract is prolonged to the extremity of the genital tubercle (phallus) and the male genital tract opens into the urinary tract (ejaculatory ducts opening in the posterior urethra).



Under the influence of a feminising sex-formative impulse the genital spur descends, separating the opening of the urinary tract from that of the genital tract.

The external genitals, occurring after the asexual embryonic phase, *i.e.*, in the 8-mm. embryo, also are first bisexual. They are characterised by a genital tubercle (phallus) on the under-surface of which is the urethral groove. The edges of this groove are the urethral folds. At the basis of the genital tubercle and separated from it by a groove are rounded lateral ridges, the labioscrotal swellings. Under the influence of a masculinising sex-formative impulse the genital tubercle develops into a penis. The urethral groove extends to the end of the penis, the glans. The urethral folds, and edges of the urethral groove, unite and thus transform the urethral groove into a canal. The separate labioscrotal swellings coalesce and form the scrotum. When the sex-formative impulse is feminine the genital tubercle develops slightly into the clitoris. The urethral groove remains at the base of the clitoris as an open vestibule. The urethral folds constitute the labia minora, the labioscrotal swellings the labia majora.

The mammae follow the same pattern. They are originally bisexual. The masculinising sex-formative impulse inhibits their development. The feminising sex-formative impulse, predominantly endocrine, allows them to develop.

The same pattern occurs in the extra-genital sexual characters. At an early stage, which comprises not only embryonic life but also post-natal development up to the adult stage, muscles, bones, fat, hair, larynx, nervous system and particularly the superior cerebral cortex, the psycho-associational cortex, are bisexual. The sex-formative impulse, transmitted through the organisers and more especially through the endocrines, masculinises all these features, developing their male potentialities and inhibiting female possibilities (or feminises them through the inverse process).

The libido develops according to the same biological pattern. Here also are the three phases of asexuality, bisexuality and unisexuality. In the asexual phase, which comprises the embryo and infant, there is no libido. The phenomena described by Freud and referring to the satisfaction arising from urination and defaecation have no connection with libido, which in a clinical sense means sexual attraction towards an individual. Narcissism is a definite phenomenon, but to speak of narcissistic libido is to

play with words and extend uselessly the significance of the term libido. Slightly before puberty the libido appears and is at first bisexual (ambivalent libido), the prepuberal child being attracted towards both sexes indifferently. This attitude has a rudimentary sexual character in the same manner as the bisexual formations of gonads, gonoducts and other organs and tissues are rudimentary. Later at puberty, but principally a little afterwards, the libido becomes unisexual, *i.e.*, of male or female type, and attraction is towards women or men respectively. At the same time this libido acquires a more distinct sexual or erotic character through erotisation of the cerebral cortex by the sexual hormones. By viewing the development of the libido in the light of the general pattern of development of the sexual characters we avoid the unnecessary metaphysical complications introduced into the question by the psycho-analysts.

Disturbances resulting in weakness of the sex-formative impulse, changes in the field or organ reactivity to that impulse (*i.e.*, to the sex ferments of the genes, the sex inductors of the organisers and the sex hormones of the endocrines) and modifications in the biological environment make for imperfect sexual differentiation of all these organs and tissues, and thus for intersexuality. For instance, a weak masculinising impulse does not inhibit completely the cortical element of the gonad, and thus ovarian tissue coexists with the testicular. The Müllerian tract is not inhibited completely, and thus vagina, tubes and uterus may develop. A defective masculinising impulse does not induce descent of the genital spur and thus separation of the openings of genital and urinary tracts. It does not allow development of the genital tubercle into a perfect penis, nor prolongation of the urethra up to the extremity of the penis, nor closure of the urethra through coalescence of the urethral folds, which thus remain as labia minora delimiting a hypospadiac urethra. It does not permit union of the labioscrotal swellings into a normal scrotum, this formation thus remaining at the stage of bifid scrotum. All other male intersexual features bearing on the extra-genital sexual components develop through the same mechanism, and female intersexual features develop analogously.

In brief, intersexual features develop through imperfect unisexualising action of the sex-formative impulse (genes, organisers, endocrines) on the bisexual self-differentiation of the biological field.

SEX IN ANIMAL EVOLUTION

Sex is a feature of the living being that promotes effective procreation and thus propagation of the species. It occurs at a relatively advanced stage of evolution. The lower living beings have no sex, and their reproduction is not effected by the encounter of male and female. At later stages of evolution sexual characters occur but male and female are united in the same plant or animal; bisexualism has succeeded the earlier stage of asexualism. Still later there is separation of the sexes, gonochorism, male features going with one set of animals, the female with another. However, this separation of sexes is never complete. Every male animal, including man, has rudimentary female features, and *vice versa*.

The question has arisen, whether the two sexes represent a simultaneous stage of evolution or whether one or the other sex represents a higher stage. Biological research seems to indicate that the latter view is correct.

In certain lower animals the female appears to be the more developed. Geoffrey Smith has suggested, as Morgan reports in his "Theory of the Gene," that if a free swimming larva barnacle becomes fixed it grows to full size, passing through the male stage to become a female, but if it attaches itself to a female it develops no further than the male stage. In higher animals the male sex seems to be the higher in evolution, and in fact experimental feminisation of a male is much more difficult than the experimental masculinisation of a female. The male sex seems more stable.

In humans, according to many biologists, the male sex shows a more perfect evolution, an idea developed by Maranon. This is shown by the fact that the castration of a male produces feminism, whereas the same operation on a female results not in masculinisation but in infantilism. It is shown also by the post-natal development of a male child, which in its early stages is infantile, *i.e.*, approximately asexual, at puberty shows some feminine features and only later, at full maturity, acquires full virility. Finally, it is shown by the fact that within certain limits women who acquire virile characters do not arouse the loathing provoked by the sight of feminised men. On the contrary, they often receive admiration. In this war women are showing qualities of leadership, daring and enterprise usually considered as male sexual characters.

The historical example of Lady Hester Stanhope is another illustration of this point. This granddaughter of Chatham and niece of Pitt was a mild adrenal female intersex. Her features and build, so like those of her famous uncle, were masculine. Although she had some sentimental and even physical adventures these were only unimportant episodes in her life, and in spite of her brilliancy and beauty, in the words of a Frenchman who met her, "Tender sentiments are those least associated with the impression she gives." Her behaviour, her enterprise, her courage and domineering tendencies were such as are linked with the male sex. However, for all that she was admired.

It is interesting to recall that when Renaissance physicians described their cases of "change of sex," whose nature they did not truly understand, they saw "change" take place from female to male, never from male to female. This because, as Ambroise Paré puts it, Nature tends always from imperfect to perfect, never from perfect to imperfect, and thus from the female to the male sex, never *vice versa*. Is this an application of La Rochefoucauld's aphorism "there is always a little glimpse of truth in many errors"? Is evolution continuing, and is the female sex developing progressively certain male features? According to Schultze, the female has been arrested in the course of evolution by canalisation of morphogenetic energy so as to realise the most complete development of the maternal organs to the detriment of the total evolution. Is it not possible that while retaining the maternal organs the female continues to evolve towards masculinity as regards other features?

CHAPTER III

PHYSIOPATHOLOGY OF INTERSEXUALITY

INTERSEXUALITY results from a disturbance of the sex-differentiating or sex-formative mechanism. When, in the days of the ancient Eastern peoples, sex was considered to be formed by divine intervention, intersexes were ascribed to Heaven (as Hippocrates relates, with some contempt, when discussing the beliefs of the Scythians). For the ancient Greeks, who regarded sex as based on the gonads, intersexuality became a gonadal disturbance. When later sex was viewed as determined by a certain endocrine balance, intersexuality was considered as an endocrine disorder. Nowadays intersexuality is ascribed to a disturbance of the complex sex-formative mechanism, already described, centring around the genetic-endocrine sex-formative impulse. In order to clarify the description, the disturbances of the various elements of this mechanism are here considered separately.

Disturbances of the Biological Field of Reactivity. Particular modes of function of the biological field, transmitted hereditarily, make for imperfect sexual differentiation. At present this is largely a matter of theoretical biology, but certain facts emerge from recent work. It is obvious in general that even given a normal sex-formative impulse of genes, organisers and endocrines, inhibition of the female potentialities and stimulation of the male potentialities of the field depend greatly on the mode of function or reactivity of that field. This has been demonstrated as regards the reactivity of the body cells to hormonal sex-formative stimulation by Albright's experiment of the Seabright-Bantam syndrome.

Disturbances of field function of reactivity may be due to various factors. In one class of case we have to accept a particular mode of field function transmitted by heredity. In another class we have to accept a particular metabolic influence of the genes modifying the reactivity of the body cells (the various elements of constitutional regulation interact). Finally, we have to accept certain environmental factors modifying the reactivity of the cells. These are not known in detail, but at an advanced stage of

ontogeny they are held to act through the vegetative nervous system.

Disturbances of the Sex-differentiating or Sex-formative Impulse. This impulse may be disturbed at its genic, organiser or endocrine phase.

A. The balance of the sex genes which makes for normal masculinising or feminising impulse may be upset. This is a question not only of the number but also of the functional power of the genes, the fermentative power of either the masculinising or feminising genes. When this genic balance is upset a weaker masculinising or feminising impulse arises, and results in an imperfectly sex-differentiated human being, an intersex. The intersexes originating in a genic disturbance are termed genetic intersexes.

Disturbance in sex gene balance or function is in general due to heredity. Certain fertilised human ova may possess sex genes defective numerically and functionally, transmitted from the parents. The same disturbance, however, can be due to environmental factors acting on the ovum. Normal sex genes may have been transmitted to that ovum through both parents, but factors resulting in metabolic disturbance of the mother can cause gene mutation and thus sex gene deficiency.

B. The organisers secrete certain sterolic hormones, more precisely called inductors, which possess a general morphogenetic function and thus contribute to the differentiation of sexual features. Each sex therefore requires a balance of masculinising and feminising inductors. Disturbance in the organisers upsets this balance and thus makes for imperfect sex differentiation. Although the rôle of the organisers in general has been studied well—the recent work of J. Needham is rich in facts illuminating this part of biology—their special rôle in the genesis of intersexuality remains at present on the theoretical plane.

C. Normal sex depends on the balance of the sex hormones which makes for preponderance of either the masculinising or the feminising hormones. When this balance is upset their masculinising or feminising action becomes inadequate, and the result is an endocrine intersex.

Hypotestosteronism in males, which allows the oestrogens normally present in males to act unchecked, causes defective masculinisation and thus male intersexuality. In certain rare and obscure cases a similar condition results from an adreno-

cortical tumour. Hyperfunction of the adrenal cortex in females, due either to an adrenocortical tumour, or to excessive antepituitary adrenotropic hormone secretion arising from a hypersecreting basophile adenoma of the pituitary, or from diencephalic disturbances affecting the adrenotropic secretion of the pituitary, makes for female intersexuality. Hypertesterinism in females due to an arrhenoblastoma also causes female intersexuality.

The endocrine disturbance can occur either during embryonic life or in the post-natal period. It may involve only an endocrine gland or glands or a whole neuro-hormonal system. It is determined by an interaction of constitutional genetic glandular inferiority and environmental factors such as infections, intoxications, dietetic insufficiency or special avitaminoses, and traumatic factors such as castration. Of recent years special significance is attached to psychogenic factors which affect the diencephalic centres of the neuro-hormonal systems and result in the development of certain post-natal intersexual states. Intrauterine glandular disturbances are caused by various factors disturbing the metabolism of the mother and thus reacting on the tissues of the embryo, including the endocrines, and by infections and intoxications involving the mother.

Disturbances of the Biological Environment. The rôle of these disturbances in the genesis of intersexuality has been delineated in the section dealing with the biological environment as part of the sex-determining mechanism. In human clinic environmental factors such as, for example, metabolic disturbances of the pregnant woman and later, dietetic and toxic factors upset the function of the sex-formative genes and endocrines. A striking clinical example is the frequency of male intersexual conditions among the badly nourished populations of the Far East.

Among environmental conditions factors of social environment and education and various psychogenic factors play an important rôle, particularly by counteracting the masculinisation or feminisation of the psyche (or, to speak organically, of the psycho-associational cortex). For example, the masculinising action of the endocrines on the psycho-associational and sexual cortex may be impeded or even deflected (sexualisation or erotisation of the cerebral cortex occurs mainly at puberty), and the boy becomes imperfectly masculine, effeminate, homosexual, a sort of psychogenic intersex.

Psychopathology of Intersexuality. The great work of Freud on the development of sexuality has furnished important elements in the general physiopathology of intersexuality. The psychopathological study of intersexuality by the psychoanalysts must be correlated with the general biological development of sex.

The essential psychological aspect of sex, studied by the psychoanalysts, is the libido. In order to thread the maze of speculations and theories which obscures the facts discovered by the psychoanalysts, the development of the libido must be viewed in parallel with that of all the sexual features.

There occurs a phase of asexuality, a phase of bisexuality and a phase of unisexuality. The process is the general process of sex differentiation, and consists in the interplay, already described, of biological field, sex-formative impulse and biological environment. The development of libido is distinguished by its occurrence in post-uterine life and by its gradual appearance throughout the years separating birth from maturity. It has been studied essentially by Freud, who used a method now ranking among scientific methods of investigation, the psychoanalytic method, and expressed this development in terms of psychology, a mode of expression also accepted in modern medicine. In general biological terms, the phase of asexuality corresponds to the phase of narcissism of the psychoanalysts. The phase of field bisexuality corresponds to the phase of ambivalent libido of the psychoanalysts. The phase of unisexuality crowns the development of the libido as well as that of the other sexual characters.

Psychological intersexuality is thus determined by the factors studied for intersexuality in general, *i e.*, by disturbances in the biological field, the sex-formative impulse and the biological environment. However, a very great rôle should be attributed to environmental disturbances such as educational factors, various sexual traumata of childhood and so on. These have been thoroughly investigated by the psychoanalysts.

The Physiopathological Division of Intersexual Conditions.
Deep Constitutional Intersexes and Endocrine Intersexes. In intersexuality the mechanism of sex determination is disturbed in its entirety, but according to the elements of this mechanism predominantly and primarily disturbed two classes can be distinguished, deep constitutional intersexes and endocrine intersexes. Although there are many intermediate forms this division is

distinctly demonstrated by clinical observations, and explains many clinical and therapeutic differences.

Deep constitutional intersexes are those in which sex reversal occurs at a very early phase of human development, the genic-organiser phase. They are determined by an interplay of (a) disturbances in the genetic sex-formative, *i.e.*, masculinising or feminising impulse, (b) disturbances in the organiser sex-formative impulse, (c) disturbances in the reactivity of the cells of the embryo.

Endocrine intersexes are those in which sex reversal occurs at the endocrine phase of human development. They result from an interplay of (a) insufficient masculinising or feminising impulse of the endocrines, (b) an abnormal reactivity of the body cells, particularly of those constituting the sexual formations.

This physiopathological distinction explains clinical differences. Deep constitutional intersexes occur very early, are intractable (but not absolutely, because by artificial endocrine regulation the insufficient genic or organiser function can be counteracted), and are often accompanied by manifestations of other deep constitutional or genetic disturbances ("stigmata of degeneration," a term embodying an exploded theory as to their mode of formation). Endocrine intersexes may occur later in life, they are more amenable to endocrine treatment, and are accompanied by other manifestations of the conditioning endocrinopathy. I emphasise this division, which although of very great practical importance has not been made until now because only recently has endocrinology been considered as correlated with constitutional medicine in general.

Endocrine intersexualisation in particular has been studied experimentally, much of the recent work having been summarised by Greene. From the numerous researches one fact emerges, namely, that early treatment of the ovum or the embryo with heterosexual hormones causes intersexualisation. The relation between genic and endocrine factors in sex has been studied by Danforth.

CHAPTER IV

THE SEXUAL CHARACTERS

THE intersex being either a male possessing certain female sexual features or a female with certain masculine features, intersexual conditions depend for clinical understanding on knowledge of sexual features or characters. All parts of the body bear the stamp of the particular sex to which the individual belongs. All morphological, functional and psychical components of the body-mind differ in man and in woman. Of these components a few show a sexual stamp so marked that they are recognised as constituting the characteristics of the particular sex. This conception of sexual characters, so useful in biology in general and in clinical medicine in particular, was introduced by John Hunter and developed later by Charles Darwin. Hunter distinguished between primary and secondary sexual characters. The former sexual features bear on the organs and functions concerned with reproduction, the latter on elements of mind and body which have nothing to do with reproduction. In other words, Hunter, like Darwin after him, distinguished between genital and extra-genital sexual characters. An unnecessary subdivision of the secondary sexual characters into secondary and tertiary was made later by Havelock Ellis.

The division advocated by Hunter and Darwin followed strictly natural historical descriptive lines. These biologists did not imply any hierarchy of sexual characters by their terms primary and secondary. Unfortunately, some physicians who followed them inferred a hierarchy, and thus believed the primary sexual characters to be more important in sexual determination than the secondary, and the secondary than the tertiary. Modern biological research, however, demonstrates that such a hierarchy cannot exist, and that all sexual characters are equal in the constitution of the particular sex. In man sex is as much in the psyche (the so-called tertiary characters) as in the gonads (the primary sexual characters). For this reason I oppose grouping into primary, secondary and tertiary, and have adopted a clinical grouping, given in the following table.

The sexual characters, *i.e.*, the special features differentiating

certain parts of the body-mind belonging to man from those of woman, have developed through the particular functions of man and woman in perpetuating the human race, and through the need of developing certain characteristics which determine the sexual appeal of male for female and *vice versa*.

After the pioneer work of John Hunter and Charles Darwin the sexual characters were studied by many biologists and clinicians. Outstanding contributions are those of Isidore Geoffroy de Saint-Hilaire, Pezard and, as regards the psychological sexual characters. Havelock Ellis

MALE	SEXUAL CHARACTERS	FEMALE
<i>Gonadal</i>		
Testis functioning.		Ovary functioning
<i>Genital</i>		
Epididymis, vas deferens, scrotum, penis, urethra of male type (enclosed in penis), seminal vesicles, prostate, rudimentary uterus (prostatic utricle), undeveloped mammae.		Labia majora and minora, clitoris (rudimentary penis), urethra of female type (perineal or hypospadiac), vagina, uterus, tubes, mammae well developed, parovary, Gartner's duct (rudimentary Wolffian duct), no prostate or seminal vesicles.
Erections, ejaculation of seminal fluid, rapid orgasm necessary for fecundation, no lactation.		Rudimentary erection of clitoris, no ejaculation, slow orgasm necessary for fecundation, lactation.
<i>Morphological</i>		
General male appearance, angular and roughly hewn.		General female appearance, round and delicate
Notable muscular relief, solid skeletal structure		Muscular relief not apparent. Delicate skeletal structure.
Skull large, with well-marked ridges and protuberances. Angular lines. Jaw strong. General expression of physiognomy definite. Canine teeth developed, lateral incisors less developed.		Skull small, with unobtrusive ridges and protuberances. Flowing lines. General expression of physiognomy indefinite. Canine teeth blunt, large central incisors.
Scapular region wide in relation to pelvis.		Scapular region narrow in relation to pelvis.
Neck short, with marked muscular and laryngeal relief (Adam's apple).		Neck long and round, without muscular or laryngeal relief.
Lower limbs straight, tendency to genu varum.		Lower limbs converge towards knees, tendency to genu valgum.
Gait energetic and straight, movements vigorous and abrupt, posture erect.		Gait slightly swinging, less vigorous movements, mannered gestures, less erect posture.
Fat localised especially on upper body except for mammae.		Fat more abundant, localised on lower body but also around mammae.
Scalp hair short, hair on face and body, upper edge of pubic hair triangular, hair coarse.		Scalp hair long, no hair on face or body except pubis and axillae, upper edge of pubic hair horizontal, hair fine.

Voice

Low pitched, baritone or bass.

High pitched, soprano.

Psychological

Libido towards women.

Libido towards men.

Instinct of social activity (defence and increase of family).

Maternal instinct. ✓

Activity directed outwards, extravert attitude.

Activity directed towards home, introvert attitude.

Tendency to creative and abstract work.

Work of imitation and precision. ✓

Emotional reactions not very marked.

Emotional reactions accentuated. ✓

Active dominating temperament.

Submissive temperament. ✓

Will to maleness

Will to femaleness ✓

DESCRIPTION OF THE SEXUAL CHARACTERS

Gonadal. The gonadal sexual character of the male is the testis, that of the female the ovary. Certain authors call the gonadal characters "fundamental," a senseless term according to the present view of sex formation. Menstruation also belongs to the gonadal characters, as it depends ultimately on the ovary. Fertility depends also on the gonads.

Genital. The genital anatomical male characters are epididymis, vas deferens, scrotum, penis with male type of urethra (enclosed completely within penis), prostate, seminal vesicles and undeveloped (male type) mammæ. The female genital characters are labia majora and minora, undeveloped penis (clitoris), female type of urethra (perineal or hypospadiac), vagina, uterus, tubes. Negative female sexual characters are absence of prostate and of seminal vesicles.

The functional male genital characters are erection, ejaculation of seminal fluid, and rapid orgasm necessary for fecundation. The female functional genital characters are slow orgasm necessary for fecundation and rudimentary erection (clitoris) without ejaculation. The sexual appetite in the male is more urgent than in the female, and thus male chastity is rarer and more difficult.

Morphological. The morphological characters are studied here in detail because of their importance. The skilled clinician is often led by them to his diagnosis. It is a pity that physicians are not more thoroughly trained in human morphology, which constitutes one of the most important elements of real diagnosis, the diagnosis of the person. As a part of my clinical teaching in Athens I used to take my students for long hours in the museums of sculpture, and believe that they benefited as much from this as from learning to count blood corpuscles.

Besides the special morphology of the genital organs including the breasts, other specially striking morphological features differentiate male from female. These features developed on the basis of the respective *rôle* of each sex in perpetuation of the race, and according to the needs of each sex in attracting a heterosexual partner.

Sex has imposed on woman the apparatus for incubation and nourishment of the offspring, and activities concentrated on the nourishment, care and protection of that offspring. Sex has taken these from man, but instead has imposed upon him apparatus for protecting and feeding the family. Thus man has developed greater skeletal and muscular ruggedness, woman a special pelvic configuration.

Man and woman offer in their habitus differential features, and thus special sexual characters referring to the habitus. Man is taller and roughly hewn, woman shorter, rounded and delicate. Muscular relief is prominent in man, principally because the muscles themselves are more developed but also because they are less covered in fat, while the smaller muscles of woman are enveloped abundantly in fat and thus confer no muscular relief.

The structure of the head differs in man and woman because of the more rugged and highly developed skeletal scaffolding of the male. Man has the larger head. Its ridges and protuberances are notable, the lines angular, the jaws strong, while the general expression of the physiognomy is definite. The canine teeth—the fighting teeth—are more developed than the central incisors. In woman, to the contrary, the skull is smaller, ridges and protuberances are less salient and the lines more flowing, with a less definite general expression of face. The canine teeth are blunt and the central incisors well developed. Altogether the female skull approaches the infantile skull.

The neck is relatively short in man, with marked muscular and laryngeal relief, the Adam's apple manifesting the greater development of the laryngeal cartilage. In woman the neck is rounder, usually longer, and shows neither muscular nor laryngeal relief.

The trunk shows the muscular relief and skeletal ruggedness usual in man. The waist, barely existent in man, is marked in woman. The lumbar region is flat in man, lordotic in woman. The gluteal regions are square and contractile in the male, voluminous and rounded in the female.

The pelvic region shows distinct differences. In man it is relatively narrow, straight, its skeleton is prominent. In woman it is wide and well covered with fat. The difference in pelvic width is shown by the ratio of biacromial and bitrochanteric diameter. In man this is 100 : 93, in woman 100 : 97. As a result man has wide shoulders in relation to the pelvis, woman a wide pelvis in relation to the shoulders.

The limbs show in the male his characteristic muscular relief and ruggedness. Legs are straight, wrists and ankles thick, and the nails, organs of fight, are substantial. In woman the limbs are more rounded. Her legs are not straight, but because of the greater pelvic width converge strongly towards the knees, in marked genu valgum. Wrists, ankles and nails are more delicate.

Differences of skeletal and muscular structure are reflected in the gait and other movements. Man's gait is straight and energetic, woman takes shorter steps and sways, the swinging being a distinct feminine sexual trait accentuated in some Spanish dances and seen also in feminised men. Man shows more abruptness and vigour in all his movements, and therefore makes a more impressive orator, for in eloquence, as Demosthenes has said, action is the first, second and third rule. The rare good woman orators I have come across made vigorous male gestures while speaking.

Fat distribution differs also in man and woman. Man is less generously supplied than woman, and shows his fat chiefly on the upper part of the body, above the umbilicus on chest and shoulders. Woman's more abundant fat gathers mainly around the pelvis and in general below the umbilicus. Adrenal obesity is a caricature of male fat distribution, fat accumulating in the supra-umbilical part of the body. Lipodystrophy, a disease exclusive to women, is a caricature of female fat distribution, such patients showing no fat at all on the upper body and normal fat on the lower parts.

Finally, hair distribution differs in man and woman, and justifies Darwin in classifying hair among the sexual characters. The hair of the scalp is less abundant in man, and even when left to develop freely never passes the shoulders, whereas female hair can reach lower than the waist (Bucura). Further, in man hair leaves the fronto-parietal angles very early in life, the resultant bareness of the forehead thus manifesting only a peculiarity of hair development and not any superior cerebral capacity.

Men's eyebrows are well developed, thick and tending to meet above the nose, while those of the female are thinner, are limited to a line and are not prolonged above the nose. From ancient times onwards women have plucked their eyebrows to accentuate this particular sexual feature. Man shows hair on the face and body, while woman has hair only in axillæ and pubis. The pubic hair of man runs upward into a point towards the umbilicus, while in woman it ends on the upper limit in a transverse line. In general male hair is thick and coarse, female delicate and silky.

The above considerations refer only to the white race, for various ethnic differences exist. Thus, in woolly-haired races men and women have equal development of scalp hair (Bushmen, for instance), and in straight-haired races such as the American Indians men show a more abundant scalp hair development than women.

The Voice. In the whole scale of animal life the voice has sexual significance. The masculine voice is low, usually an octave lower than in woman. The difference between this and the female soprano arises from the different development of the larynx. Man's larynx is more fully developed and his vocal cords are 18 mm. long. Woman's larynx approaches the infantile, and her vocal cords have an average length of 13 mm. The tenor voice in man is thus a sign of feminisation, and a contralto voice in woman denotes masculinisation.

Psychological. The essential psychological sexual characters fall into four groups, (a) the libido, (b) general activities, (c) the sexual mannerisms, (d) the will to maleness or femaleness.

A. In the male, libido or sexual attraction is directed towards the female, and in the female towards the male. Thus libido is of male or female type. It is not a purely psychological feature—no biological phenomenon is ever purely psychological—but in man it is distinctly telencephalised and thus can be ranged among the psychological characters.

B. The general activities of humans show certain differences according to the sex. Man possesses an instinct of social activities (defence and increase of the family). His activities are directed outwards and his attitude is thus extravert. His tendency is towards creative and abstract work. His emotional reactions are not very strong. His temperament is active and dominating. In contrast, woman's activities are directed towards the home, her

attitude is introvert and her instinct maternal. Her work tends more to imitation and precision. Her emotional reactions are emphatic, and her temperament is submissive.

Man was originally the hunter of food and the protector of the family. This developed essentially in him the will to power, shown to be a basic biological law by the ancient Greek sophists, and romanticised in modern times by Nietzsche. For this reason his activities are directed outwards, the extravert attitude being essentially male. As he had to be efficient in fight he developed mastery over his emotions and an active and dominating temperament. However, social developments have removed the need for man to hunt for food and, in usual circumstances, to engage in direct fight for the protection of his family. His will to power and fighting activities have taken the form of intellectual activities of a creative constructive nature.

Woman was originally the nurse and protector of the offspring. For this reason her emotional and tender side has developed and her activity has turned inwards, the introvert attitude being an essentially feminine attitude. For the same reason her temperament is passive and submissive. Here again evolution of these primitive features is due to social developments. The intellectual powers have developed less than in man as a creative constructive urge but have become imitative (the statistics of art museums, according to Gomez Ocana, show that the great majority of copyists are women). The intellect of women has adapted itself more to social activities bearing a relation to their original destiny of nursing and domestic care. Hence woman is more suited than man for teaching, caring for the sick and for certain industries, professions and arts which require manual dexterity and careful attention.

All this explains the intellectual differences between man and woman, and shows that woman's intellect is not the inferior power that the Leipzig neurologist Moebius deemed it, but is different from that of man. It is not creative, and whenever a creative intellect exists in woman it is an intersexual feature. Nietzsche has written in one of his works, "When a woman has scientific talents there is something ill defined in her sexuality."

Does this difference of mental capacity between man and woman justify the attitude of the anti-feminists? Are the arguments underlying this attitude, put forward by Weininger, Moebius, Metschnikoff, Maranon, biologically sound? I do not

think so. These authors forget the essential biological law, that sexual features are neither fixed nor stereotyped but in process of evolution. The male intellect has developed as such through evolution, and in the same manner the female intellect; but evolution continues, and it is possible that through environmental conditions the female intellect and temperament approach the male more and more nearly.

C. The sexual mannerisms carry out in man and woman the purpose of sex attraction. It seems that woman needs more such artifices than man. In his "*Femme de Trente Ans*" Balzac says that Nature created the female, Man the feminine. The love of adornment and clothes, the cultivation of fascinating mannerisms which occupy so much of woman's time and attention, are seen, often in caricatural exaggeration, in feminised man.

D. Dominating all sexual psychological features, however, is the will to sex. Man wills to be a male and act as a male. Woman wills to be female. We could paraphrase for sex the title of Schopenhauer's famous work, and speak of "Sex as Will and Idea." It is to be remarked, however, that the will to the female sex in woman is less strong than man's will to maleness. Frequently woman shows a desire of maleness, which in neurotic conditions takes the form of what Adler has called the masculine protest.

The Balance Sheet of Sexual Characters. Intersexual conditions can be understood more clearly by means of a method which could be termed the balance sheet of sexual characters. For each individual a sheet is filled in, one column comprising the male features, the other the female features. For the normal male the male column is full and the female column contains only a few rudimentary features, the contrary occurring in the case of a "normal" female. The male column for a male individual is called protosexual, the female column heterosexual or intersexual.

The Genetic Sex. The genetic sex is that of the initial genetic sex-formative impulse. It is the real sex, and according to it intersexuals are classified.

The ideal clinical determination of the genetic sex would be based on knowledge that in the individual under examination a masculinising or a feminising impulse originated in his sex genes. This is of course impossible, and the genetic sex is judged by the results of the genetic sex-formative impulse. These are all the sexual characters, as shown in the balance sheet of these features.

Normally certain of these characters such as the presence of testis in man and the special configuration of the genital organs in both sexes weigh the balance in favour of maleness or femaleness. Genetic sex determination is then easy, and for practical purposes sex is registered at birth according to scrutiny of the external genitals. In intersexual conditions, however, this genetic determination is difficult, and the balance sheet of sexual characters needs careful scrutiny, not numerical consideration.

Sex is a whole, and in biology a whole does not mean the sum of its parts but an integrated being. Thus features belonging to the highest integrative process, the cerebrum, must often dominate in judgment. Sex is in the psyche as much as in the gonads or the morphology, for in the last resort man is integrated into a whole by the psycho-associational cortex. The psychological features, however, including the will to maleness or femaleness, must not be given absolute decision in determining the genetic sex, for the psycho-associational cortex as well as the gonads can be intersexualised. In some intersexes the genetic sex can, by the method of the balance of sexual characters, be assessed with precision. But in others decision is impossible, and in such states the sex is said to be undetermined. This means that the genetic sex is undetermined, but as these unfortunate individuals cannot be left to go through life sexually undetermined their pragmatic sex has to be accepted.

The Pragmatic Sex is that indicated by the will of the patient. It is the sex that will make him happier and confer better adaptation. The term derives from pragmatism, based on the old principle of Protagoras, that "the measure of everything is man" and the modern one of Peirce that "every truth has practical consequences and these are the test of truth." Unconscious of it though we may be, the principles of pragmatism dominate sound clinical work.

The pragmatic sex is to be accepted in cases of severe intersexualisation, in which the genetic sex is very doubtful and cannot be discovered. These individuals must have their place in the sun, and can have it only by virtue of their will to a particular sex. Otherwise they would be abandoned as a class apart of "undetermined sex." Many will object that the sex they will may not be their true, *i.e.*, genetic sex, but in such cases the sex that brings most happiness and the best adaptation is surely the true sex.

The pragmatic sex merits acceptance also from the social and medical standpoints for those severe intersexes (those with intersexualisation of the genital organs) whose will opposes the objectively determined genetic sex. When such persons are forced into their unwanted genetic sex (and it must be remembered that despite even high probability, there is no certainty in determination of the genetic sex) their life is indeed miserable and many of them commit suicide. By maintaining for them the sex that they will we make them happier and better adapted without inconvenience to others. Even in the sixteenth century, as Ambroise Paré tells us, a hermaphrodite had the right to choose his own sex. Such individuals should be considered male or female according to their will, and it is the task of the surgeon to perfect the sex they choose. The only exceptions are cases of malignant neoplastic intersexuality, in which the neoplastic indication overrules the intersexual element.

The pragmatic sex cannot be accepted socially, legally or medically for a morphological or psychological intersex, *i.e.*, one in whom intersexualisation bears only on the morphological or psychological features, the genetic sex being indicated decisively by the gonads and genital organs. Neither can it be accepted for certain mild genital intersexes such as hypospadiacs and gynecomasts, for practical reasons. A man from all other points of view cannot be allowed to consider himself a female if by any mental aberration he wishes to adopt the female sex. A male homosexual, male in morphology and work, cannot be excused for his practices simply because he wills, at all events in his sexual behaviour, to be a female. Even if male homosexuals or male transvestists live unhappily and commit suicide when thwarted, overwhelming social considerations oblige the physician to ignore their will and thus their pragmatic sex. A male homosexual, for example, is a source of moral depravity in a group of other persons, particularly at schools. Besides being a generally depraving influence he is a source of contagion of intersexuality. He must therefore be thwarted in his activities, although more by treatment than by punishment. Morphological, psychological and mild genetic intersexes thus differ from severe genital intersexes who are not sources of social infection and intersexuality, whose problem is individual, whose misfortune lies within themselves, and who by being allowed into the sex they will can be made happier and more useful without any damage to others.

In the third century of our era the great Roman jurist Ulpianus introduced the fundamental principle of legislation concerning intersexes by laying down that for every intersex the prevailing sex should be accepted, and thus that the intersex should be treated socially and legally according to the prevailing sex. "*Quæritur hermaphroditum cui comparari? et majus puto ejus sexus æstimandum qui in eo prævalet.*" The question is how to determine which sex prevails in an intersex. According to the principles developed above, the prevailing sex of an intersexual individual is the genetic sex in extra-genital and mildly genital intersexes, and the pragmatic sex in severe genital and gonadal intersexes.

CHAPTER V

FEMINISM

(MORPHO-PSYCHOLOGICAL ANDROGYNOIDISM;

"Unseemly woman in a seeming man," SHAKESPEARE, ROMEO AND JULIET

THE nosography of natural history of male and of female intersexual conditions has passed through four phases, the biotypological, the teratological-mythological, the anatomoclinical and the biological physiopathological. The last is the contemporary phase.

The biotypological phase was that of the ancient Greeks, who described intersexes as special types of humans—biotypes would be the term used to-day. On these lines Hippocrates depicted the conditions known to-day as feminism and virilism (morpho-psychological intersexes). Aretaios described gynecomasts and Aristotle male hypospades, indicating the feminine nature of their anomalies.

The teratological-mythological phase began with Pliny, developed during the Renaissance with Ambroise Paré, Paolo Zacchia, Jacques Duval, Johannes Wier and others, and extended into the eighteenth century with Georges Arnaud. Unlike the Greeks, the physicians of this period studied human intersexes as freaks of Nature, as monsters rather than as types of human constitution, and for this reason they dwelt on the severe forms of intersexuality. This teratological point of view deprived their descriptions of the clinical accuracy of the Greeks and turned them into fairy-tales, accepted uncritically, related in a manner rivalling that of the Thousand and One Nights, and thus useless from the scientific point of view. This long period has been called by Isidore Geoffroy de Saint-Hilaire the period of teratological fables.

The anatomoclinical-natural historical phase occurred in the nineteenth century. Following the general principles dominating medical work in those days, intersexual conditions were described as "diseases," as morbid entities isolated on the basis of clinical and anatomoclinical features and classified, as zoologists and

botanists classify animals and plants, under appropriate labels in the glass cases of a natural history museum. Despite the irrationality of the nosographical principle as a principle of absolute knowledge, this period marks a definite progress by virtue of the accuracy of the anatomoclinical descriptions. Intersexuality was studied on these lines by Lorain, by Isidore Geoffroy de Saint-Hilaire with characteristic French clinical finesse, by the Swiss Klebs, and regarding psychological intersexes by the Viennese Krafft-Ebing, and principally by the Jew Magnus Hirschfeld—a recent victim of German persecution. Neugebauer of Warsaw collated the work belonging to this period in his bulky volumes of *Hermaphroditism* published in 1908.

The biological-physiopathological phase dominates the study of intersexuality in modern times. The introduction of general biological principles into medicine enables us to understand the human intersex as the Greeks understood it, as a special mode of psychophysical construction of the human being, a particular constitutional type of biotype, and thus to link it with the normal or ideal biotype of which it represents a simple variation or deviation. Progress in physiopathology, knowledge of the system of constitutional regulation composed of genes, organisers, psyche and neuro-endocrine system and of nutritive and environmental factors, enable us to understand the mechanism of constitutional variations and deviations. The necessity of a nosographical classification, however, is maintained, notwithstanding the attempts of the German so-called "physiological" school of the nineteenth century—an unfortunate and disastrous reaction of Teutonic obscurity against the clarity of Greek, French, British and Viennese clinicians. We group types of intersexes showing similar clinical features based on definite physiopathological disturbances of the system of constitutional regulation, and describe them as "constitutional diseases." This contemporary period of the study of intersexuality is essentially therapeutic. In fact, the biotypological standpoint of the ancient Greeks and the teratological considerations of the Renaissance physicians were devoid of any attempt at therapy, and the anatomoclinical considerations of the nineteenth century resulted only in certain local surgical procedures. The physiopathological considerations of to-day, however, and in particular the progress in psychopathology (the great work of Freud), endocrinology and metabolism, give us the general lines of therapeutic handling. It is

difficult to cite the workers who have contributed to the modern phase of the study of intersexuality. Many of them are quoted in this book, but this is perhaps the place to remember the work done in three Mediterranean centres in the years following the first world war, in Madrid by Maranon, in Rome by Pende, in Athens by myself, when we dreamed of reintroducing the Mediterranean spirit into medicine.

General Classification of Intersexual Conditions. The results of biological experiments in intersexualisation make possible a better arrangement of clinical knowledge than the cumbersome nosography of Klebs' type, which unfortunately dominates our textbooks even to-day. The following is the basis of classification of male intersexual conditions, which applies also to female intersexualities by changing the sex.

When a genetically male embryo is feminised experimentally, various degrees of intersexuality are produced according to the intensity of the feminising factor and certain conditions of receptivity. A mild process of feminisation results in intersexualisation or feminisation of the extra-genital sexual characters only. With a more intensive feminising process the external genitals are feminised. With an even greater feminising factor the gonads themselves are feminised, first incompletely (the animal involved showing ovarian tissue as well as testis), later completely if the feminising factor is intensified still further (the genetically male animal developing ovaries but no testis).

Clinical observations need arrangement according to this biological experimental gradation, if male intersexuality is to be understood more completely. First will be described the male intersexes in whom feminisation bears on the extra-genital sexual characters (morphological and psychological features, and voice), the genital organs and gonads remaining masculine. The next section deals with male intersexes whose external genitals and genital tract have become feminised, the gonads remaining masculine. Lastly come male intersexes in whom even the gonads are feminised, usually incompletely, the individual possessing a more or less well-developed ovary as well as a testis (the old "true hermaphrodite"). Whether in humans male intersexualism reaches the degree of feminisation in which both gonads are involved we do not know.

Thus according to the degree of feminisation the following male intersexual biotypes can be described.

A. Morpho-psychological androgynoidism or feminism, feminisation bearing on morphological and psychological features.

B. Breast androgynoidism or gynecomastia, feminisation involving the breast.

C. Genital androgynoidism (the old male pseudo-hermaphroditism), feminisation involving also the genital organs and tract.

D. Gonadal androgynoidism (included in the old "true hermaphroditism"), feminisation reaching the gonads.

These can be described as constitutional diseases, *i.e.* as diseases based on a disturbance of the system of constitutional regulation. They can be subdivided into various forms according to the particular mode of dysfunction of this system, according to the component of this system (genes, psyche, endocrines, environmental factors) primarily and principally involved.

DEEP CONSTITUTIONAL FÉMINISM

Feminism or morpho-psychological androgynoidism represents the first degree of intersexualisation of the male. Feminisation bears on the morphological and psychological characters. According to the modality of the physiopathological mechanism a deep constitutional feminism, an endocrine hypotestosteronic feminism and, for some authors, an endocrine thymogenic feminism can be distinguished. The clinical syndrome of complete feminism was described first by Hippocrates, who had observed it among the Scythians; Théophile de Bordeu in the eighteenth century and principally Lorain in the early nineteenth century completed the Hippocratic description. The hypotestosteronic physiopathology of one group of feminisms was introduced by Hippocrates but developed mainly after discovery of the internal secretions of the testis. The deep constitutional physiopathology of another group of feminisms emerges from recent work.

In deep constitutional feminism the sex reversal occurs at the earliest, the genetic-organiser, phase of human development. It is thus due to disturbance of the genetic or organiser masculinising impulse and to abnormalities in the reactivity of the cells of the embryo. All these are caused by hereditary factors and also by environmental factors consisting mainly in metabolic disturbances of the mother during pregnancy.

The Common Form. The morphological features dominate. The face has the soft flowing lines and mild expression associated

with women. The pelvis is wide and the hips have rounded feminine contours. The shoulders appear narrow in relation to the pelvis. The breasts are well developed and approach the female type. Fat is of female distribution, relatively abundant in the girdle region. Muscularity is poor, and the muscular relief usual in males is lacking. Corresponding to the feminine habitus a feminised swinging gait is often noted. Body proportions are normal, in contrast to endocrine (hypotestosteronic) feminism, and the whole gives a certain impression of beauty. The voice may be feminine, but less frequently than in hypotestosteronic feminism.

Gonadal and genital characters are normally male. Libido, however, is arrested either at the narcissistic (asexual) phase or at the ambivalent phase. There is thus a certain degree of passive homosexuality. The general psychology also approaches that of women.

This condition persists throughout life. It is more of a particular biotype than a "disease."

The female morphological features may be more accentuated on one side of the body. This unilateral intersexuality, depending on a special reactivity of the cells of one part of the body, is an interesting phenomenon encountered in all degrees of human intersexualisation and thus in all forms of intersexuality.

The Dilettante Form. In this form intersexualisation bears on certain psychological features. Morphologically these individuals show in some degree the features of the common form. Their psychology, however, is characteristic. They are great talkers, emotionalists, dilettantes. The typical male psychology is one of will to power, mastery of emotion, work towards a direct and external object. The opposite features, when seen in men, give the stamp of intersexuality, and in such individuals are found other feminine features, particularly morphological. Again there becomes evident a gradual transition from the normal male (with very little intersexuality, thus little psychological femininity) to more clinically distinct intersexes.

Balzac, that great psychologist, used to term *eunuques de l'art* those poets and writers always surrounded by a court of admirers and productive of nothing but talk for the sake of talking. There was in the *causeur* of the old French salons an element of intersexuality. In point of fact the physician skilled in morphology can detect in such persons female morphological

features. The muscular relief is not distinct. Fat often appears around the pelvis. The skin is white and delicate. The body and face show very little hair, while the scalp hair is very abundant. Possibly the long hair cultivated by certain artists has an intersexual meaning, although in many cases it is nothing but imitation and pose. Sexually these individuals are not markedly potent as males, although they talk volubly about sex. In some of them there is a tendency, usually Platonic, to homosexuality.

To these male psychological intersexuals Maranon has added the Don Juans. The general view is that Don Juans have an excess of virility, but I think that the fine psychological acumen of the Spanish endocrinologist is right. The Don Juans show in effect the emotional sexual instability and restless search after emotion, that are more female than male features. Since I read the work of Maranon I have in fact noted female morphological features in Don Juans.

The Male Transvestist Form. Male transvestists, finely described by Magnus Hirschfeld, represent a higher degree of male psychological intersexualisation. Such individuals are males evincing an impulse to feminine dress and care in adornment. The notorious eighteenth-century adventurer, the Chevalier D'Eon, is a brilliant historical example. He was basically a male. His genital organs, examined after his death by the British surgeon Copeland, were distinctly male. He had love adventures as a male. He was a brave soldier, was decorated on the field of battle, and showed that daring and enterprise in war usually associated with the male sex. However, as intersexual feminine feature he had a great love of feminine clothing and adornment. So successful was he in his transvestism that Louis XV employed him on a secret mission to Russia, where dressed as a woman he managed to become reader to the Empress Elizabeth and one of the most influential court "ladies." So marked were feminine traits in the Chevalier d'Eon that he was regarded as a female hermaphrodite and his king forced him to dress as a woman and take his place in the female sex. The term "Eonism" is applied by Havelock Ellis to male transvestists.

The Male Homosexual Form. Male homosexuals represent a higher degree of male psychological intersexuality. In such persons feminisation affects the libido, and they are thus attracted ~~sexually~~ to males, not to females. The intersexual nature of male

PLATE II



3 Male transvestist ('portraits of the Chevalier d'Eon in male and f male clothing).

PLATE III



4 Male psychological intersex (Oscar Wilde).

homosexuality was first pointed out by the jurist Ulrich, himself a homosexual, who in 1862 defined such individuals as "*anima mulieris in corpore virile inclusa*." It was Krafft-Ebing, however, who demonstrated distinctly the intersexual nature of male homosexuality by showing the existence of other feminine traits in this condition. It should be remembered that not all male homosexuals are of intersexual nature. The homosexuality of the ancient Greeks, for example, originated in certain social and educational conditions; it was in fact their "fagging system." Other cases of homosexuality are due to excessive virility demanding satisfaction by various means, and to communal life among men which precludes satisfaction of the sexual instinct with women. Oscar Wilde was wrong to defend his practices by referring to ancient Hellas, because his homosexuality was of definitely intersexual nature, as shown by the general emotional make-up of the poet. It was thus a source of social mischief and had no link with the homosexuality of ancient Greece, a social and up to a point useful institution within that civilisation.

Male homosexuals of intersexual origin show certain other psychological female traits. They are emotional, temperamental, unstable, artistic yet incapable of creative work. The will is not very strong, but except for the libido such individuals usually prefer to consider themselves males.

Morphological features as well as voice are generally feminised. The hips are wide. Muscular relief is absent through the abundance of fat and the lack of muscular development. The breasts are often of female type, and Krafft-Ebing even reports a case of lactation in a homosexual. Feminine mannerisms complete the picture. Transvestism often complicates it.

The genital organs are distinctly male. Testes exist and function properly, but according to Wright they seem to secrete much more oestrin than normally.

The Masochistic Form. This represents a very high degree of psychological intersexualisation. Masochists are males whose libido is feminised in such a manner that they show female submissiveness in their sexual behaviour (often of exaggerated degree) instead of male aggressiveness. Krafft-Ebing was the first to describe such patients and to indicate their intersexual nature. The term derives from the name of the Austrian writer, Sacher Masoch, who delineated many such beings in his novels.

General Course of Deep Constitutional Feministic Conditions. Deep constitutional feministic conditions are essentially chronic. Their onset is linked with post-puberal development. They progress up to a certain point and then become fixed for life. There is no spontaneous remission. Certain environmental conditions accentuate or inhibit the development of feministic manifestations, particularly the psychological feministic manifestations.

For the clinician the significance of deep constitutional feminism lies in the maladaptation to various conditions of life (*e.g.*, the marital state) shown by such individuals, and in their predisposition to various diseases following the disturbance of their early constitutional development. Of the latter psychoses are the most important, but it is also interesting to note that deep constitutional feminism is seen in individuals with disseminated sclerosis.

HYPOTESTOSTERONIC FEMINISM

In hypotestosteronic feminism the sex reversal occurs at the endocrine phase of human development, and is determined by deficiency of the masculinising impulse represented by the secretion of the interstitial gland, deficiency of the testosterone neuronal-hormonal system. This allows male oestrin to act unchecked.

The Common Form. This form of hypotestosteronic feminism is part of a more complex disease representing deficiency of the testosterone system. It is thus part of male eunuchoidism, of male eunuchism (castration disease) and of adiposogenital dystrophy (Babinski-Fröhlich disease). Thus the morphological features of hypotestosteronic feminism are in general those of deep constitutional feminism (general feminine aspect), but to them are added features depending on the basic disease—eunuchoid macroskelia in eunuchoidism and eunuchism, and the special obesity in Babinski-Fröhlich disease. The sexual syndrome is characterised by hypoplasia of the external genitals. Cryptorchidism is frequent. Potency and libido are deficient, and in some cases libido is of female type (male homosexuality).

The general psychology is feminine, and female mannerisms are often seen. Infantile traits indicate the basic hypotestosteronism.

Hypotestosteronic feminism is less intractable than deep constitutional feminism. It can retrocede spontaneously with

amelioration of the testicular function after puberty, and retrocedes also with endocrinotherapy.

A special variety of hypotestosteronic feminism is that encountered in boys showing the clinical syndrome described as "status thymicolymphaticus."

The Psychological Forms. Psychological forms are encountered similar to those described for deep constitutional feminism, thus a dilettante, a transvestist, a male homosexual and masochistic form. Their clinical features resemble those of the corresponding forms of deep constitutional feminism, except that general manifestations of eunuchoidism or of Babinski-Frohlich disease co-exist. They are less intractable.

GENERAL THERAPEUTICS OF FEMINISM

Both feminism and virilism, the so-called mild intersexual conditions, are very frequent. Many "neurotic" conditions, many social maladaptations, marital incompatibilities and behaviour disturbances are due to this constitutional inadequacy. From the social as well as the individual point of view prevention and cure of this form of intersexuality are necessary. It should be remembered that those intersexes to whom our fathers applied the description "mild," *i.e.*, feminisms and virilisms, are by far the most important from a medical point of view. In fact they are not mild, because the effects of this form of the disease are often much graver than those of the genital and gonadal intersexes—the old pseudo-hermaphrodites and hermaphrodites described as "severe intersexes" in older text-books, to which the attention of physicians was mainly directed until a few years ago. Extra-genital intersexualities occasion much greater misery, maladaptation and behaviour disturbances.

Just as slight errors of refraction cause more headache and trouble in reading than gross errors more easily corrected by glasses, the "mild" intersexualities have greater consequences than the rare severe forms, in which the problem of adaptation is simpler and can be helped radically by surgical intervention. In the so-called "mild" or extra-genital intersexes there arise the liveliest inferiority complexes, sexual and emotional difficulties in married life, inability to work, and various neurotic conditions based on the intersexuality. It is these patients who need the strongest encouragement, the

deepest understanding, the most careful guidance and the most active organic treatment.

We are far from powerless even in deep constitutional conditions. A normal deep constitutional factor, a normal genic and organiser function can be thwarted during development by an interplay of abnormal endocrine and environmental factors, and a constitutional disease thus arises. In the same manner the use of appropriate endocrine and environmental factors can correct an abnormal genetic and organiser impulse. Even in deep constitutional diseases we can succeed with our Art, whose object, as Corvisart used to say, is not always to cure the patient but to render him more comfortable and happier, in other words, better adapted. It is time to abandon the fatalistic outlook bound up with deep constitutional diseases.

Endocrinotherapy. In the present stage of science this is the most important method of treating feminism. Success, which is often remarkable, depends on skilful application, and this demands an exact knowledge of endocrine and metabolic physiology, clinical acumen and time.

The preparations most frequently used are testosterone, chorionic gonadotropin, adrenal cortex, total anterior pituitary, total pituitary gland and, in certain cases, thyroid. To these are added two important vitamins necessary to the normal working of the gonadal systems, vitamin B₁ and vitamin E, and certain constitutional medicines such as phosphorus, iron, calcium and sedatives, all of which are necessary to re-establish the balance of the body-mind.

The choice of preparations, the dosage, the mode of combination depend on individual indications, *i.e.*, on the diagnosis of the person, that highest form of medical diagnosis which I have attempted to delineate in a previous work.¹ The following up of this therapy depends on the reactions of the individual patient, judged according to the principles of this "diagnosis of the person." This procedure is essentially clinical, laboratory measures constituting only one element to be assessed in the light of the whole clinical picture. Endocrinotherapy must thus be employed according to the clinical empirical method.

It should be remembered that endocrine preparations, vitamins and certain constitutional medicines are regulators of body

¹ Modern Therapeutics of Internal Diseases, A. P. Cawadias.

chemistry, of metabolism. They are directed to the whole of the patient, and thus their indications and the following up of their results are based on appraisal of the whole of the patient, which is possible only with the clinical empirical method.

On the basis of a complete "diagnosis of the person," which includes assessment of the mode of function of all organs and systems, and the determination of the mode of function of the regulators of constitution and metabolism (psyche, nervous vegetative system, neuro-endocrine system), a first indication of the appropriate endocrine preparation is obtained. The first dosage is fixed and applied, and its effects are ascertained by the clinical following up. According to the results of this following up, which refers to total reactions, the dosage is increased or decreased or another combination of hormones is used. On this point endocrinotherapy differs from other forms of internistic treatment. The action of digitalis can be followed by concentrated attention on the heart and arteries, but the action of testosterone or thyroid cannot be followed by limiting consideration to one system or organ. Furthermore, other pharmaceutical treatments can be fixed in sufficient detail as to form of preparation, dosage and duration of treatment. Not so endocrinotherapy, in which only approximate directions can be given, the application of the treatment depending on the clinical following up of the total reactions of the patient.

Total reactions include the mental as well as the physical, and thus psychological following up is important, especially as the cerebral cortex is the most delicate reagent to hormone administration. Physical reactions are appreciated in great part by means of the general appearance of the patient, his mode of reacting to environmental factors such as temperature and physical and mental effort. They are appreciated by the manner of walking and talking, the colour and texture of the skin, the expression of the eyes, by a large number of such general manifestations as well as by a more detailed organic exploration. There is much in this exploration that recalls the detective work of Sherlock Holmes. There are no short cuts. The laudable attempt to base endocrinotherapy on certain "rational" laboratory procedures has failed even for such clear-cut cases as thyroid treatment controlled by basal metabolic determination. Laboratory procedures can help clinical exploration but can never replace it. This is not only a fact of common experience but also the

teaching of history ever since the days of Hippocrates' successors, the λογιστοί or rationalists, who were the first to attempt a "rational" therapeutics which proved as ineffective as that of all their following down to the present day. It has been said that therapeutics cannot be taught completely because so much depends on the personality of the physician. Probably this is nowhere so true as in endocrinotherapy, where success depends on the personal skill of the physician in grasping the total reactions of the patient just as success in surgery depends on the personal skill of the surgeon.

With these reserves testosterone can be indicated as the most potent virilising hormone, and in combination with vitamin B₁, vitamin E and certain phosphorus preparations it gives the best results. I have been taxed with excessive enthusiasm for this method of treatment, but those who have seen loathsome feminised boys transformed into virile adolescents by a definitely indicated hormonotherapy combined with other constitutional procedures on the basis of an accurate "diagnosis of the person" will share my enthusiasm.

Psychotherapy is the next most important method of treatment of intersexual states. It is a major constitutional procedure, and internists specialising in metabolic diseases should be skilled psychotherapists. The medical profession has taken some time to discover that man has a mind, that the mind plays a great part in disease, and that by acting on the mind we can influence the course of disease. We would have been quicker to appreciate the part of psychotherapy had we reflected more on the fact that great physicians of the past treated their patients as successfully as we do our own—if not more so. As they had not our accurate scientific knowledge their therapeutic success could have been due only to their psychotherapeutic handling.

Much can be done for intersexes by an internist with knowledge of the human soul and power to influence it towards solution of its conflicts, towards better adaptation to environment. The method to be followed cannot, of course, be described. It depends in part on knowledge of the psychological mechanisms, taught so inadequately in our schools. It depends principally on the psychological intuition and powers of leadership of the physician, qualities which although innate can be developed greatly by wide humanistic classical culture, the mainstay of the practice of all great clinicians throughout the ages.

Educational methods are important from the preventive as well as therapeutic point of view. To encourage virility in a boy and femininity in a girl is the object. Boys and girls showing tendencies to intersexuality, physical and psychological, should receive a careful education in this respect. No hard and fast rules can be laid down, for every case should be judged by itself. It can be said in general that, as I have witnessed myself, a soft sentimental education of boys leads to intersexuality, particularly of a homosexual nature. Punishment is not beneficial; explanation and real guidance are necessary. Above all, intersexuality can be prevented to a large extent if we abandon totally the hypocrisy with which sex is presented to the young, and replace the mystery of sex by the truth of sex.

Besides the usual psychotherapy of leadership, encouragement and understanding which the internist of psychological acumen employs while treating his patients organically, and besides educational procedures, deep psychotherapeutic or psycho-analytical methods enter into consideration. I must admit that I have seen very poor results from such methods. I have noticed that they tend even to accentuate the introversion so morbidly developed in intersexes. That a psychotherapist skilled in these methods could help is possible, but only in collaboration with the internist, who applies the more tangible and active organic methods. Unity of command is necessary in treatment of constitutional and metabolic disorders, division is disastrous. Intersexuality, like all other diseases, is a total reaction of the individual. It is thus physical as much as psychological, and the exclusive stress on the psychological aspect which seems so prevalent to-day is as irrational as the exclusive stress on the physical side shown by our fathers.

Physiotherapy, Dietotherapy and Constitutional Pharmaceutical Methods. These methods enter next into consideration. The fact that faulty hygiene and nutrition favour the genesis of intersexual conditions is seen by the frequency of such conditions among the poorer classes and the coolies of the Far East, and this shows the importance of procedures that aim at raising the constitution and vitality of the individual.

Physical methods act on the whole body, or rather on the whole body-mind. Their central point of action are the nerve centres of the neuro-visceral system (the vegetative nervous system) and of the neuro-metabolic system (the nervous regulators

of the endocrine glands, or more precisely the nervous components of the neuro-endocrine system'. These methods stimulate also the endocrine function of the skin (Cawadias) and thus act on the endocrine sex-formative mechanisms. At present the only known fact is that young men showing eunuchoid proportions and feminism improve with ultra-violet irradiation. French workers with Dausset have begun to develop a method of stimulating the endocrines through diathermy but there is not as yet much work on this subject.

An adequate diet is necessary to intersexes. Certain vitamins help endocrine function, and vitamin E in particular stands in some relation to the luteostimulin (prolan B)-testosterone or progestin system and would thus be masculinising. But here we enter into the domain of theory.

Therapeutics of Homosexuality

The general attitude towards male homosexuals is changing. The Jews killed their male homosexuals because they were guilty of an act prejudicial to an increase of population, and the Jews wanted much human material for the care of their flocks. The Greeks, who did not desire wholesale multiplication of their race, permitted homosexuality, albeit this was more an aesthetic homosexuality than a sexual abnormality. In Christian times the Jewish attitude to homosexuality was re-introduced and coloured the legislation of various countries. Nowadays homosexuals are regarded as sick people. This does not mean that all legal measures against them should be rejected. Male homosexuality is a social evil. The homosexual is a focus of infection of intersexuality and moral depravity, and therefore social, *i.e.*, legal measures must be taken. These measures, however, must be mitigated by medical considerations.

Much can be done from the preventive point of view. Educational measures are important. Homosexuals are usually "mother's darlings," and an effeminate education should be avoided. Sexual education, replacement of the mystery of sex by the truth about sex, is an important preventive measure. Conditions favouring homosexuality, *i.e.*, herding boys together in schools and universities without supervision from this point of view, should be avoided. Greater sexual freedom for young men such as reigns at certain Continental universities, and a more timely intervention of woman in their lives are other good

preventive measures. Homosexuals have often been saved from their tendency by a mistress or wife. The problem is thorny but must be faced.

Deep constitutional homosexuality is very resistant to treatment. Psychoanalytical methods have been used but have often resulted in suicide, and their value on the whole is questionable. Psychotherapy, in the form described in the previous subchapter, is useful. Testicular organotherapy has been applied in the form of testicular grafts but is in my opinion dangerous, and in fact libido may be accentuated in the homosexual direction. The same can result from testosterone injections. As, however, distinction between deep constitutional homosexuality and endocrine homosexuality is not usually possible testosterone may be tried, with a careful following up of the results. The best method of treating such individuals is to strengthen their constitution by an intensive parenteral vitamin therapy and to employ psychotherapeutic measures. Only mild cases are susceptible to treatment.

Treatment is more effective in endocrine homosexuality, and here testosterone treatment can be more effective.

Example of Balance of Sexual Characters in a Case of Feminism (R.R., 18)

PROTOSEXUAL (MALE)	INTERSEXUAL (FEMALE)
Testes. Penis, scrotum, seminal vesicles, mammae of male type Potency diminished	Feminine habitus. No muscular relief. Fat of female distribution abundant around pelvis. Hair of female distribu- tion abundant on head, absent from face and body except for axillæ and pubis, where form is feminine. Voice of female type. Will to be male. Libido towards women but not marked.
	Emotionality accentuated, introvert temperament, passive attitude.

CHAPTER VI GYNECOMASTIA

(MAMMARY ANDROGYNOIDISM)

GYNECOMASTIA, first described by Paulos of Ægina, represents a feminising process in a genetic male concentrated on the mammæ. Such individuals are male but possess a female breast. Various degrees can be encountered from a mild development of the adipose tissue surrounding the rudimentary male gland (adiposomastia) through development of a glandular female breast tissue (real gynecomastia) to a complete female lactating breast. The condition can be unilateral or bilateral. In the condition here studied feminisation of the breast is the predominant manifestation of intersexuality, but there are cases in which gynecomastia is part of a more general intersexualising process.

Deep Constitutional Gynecomastia. There are male individuals normal from all points of view except for their breasts, one or both being of large female type. In such cases we have to postulate either a defective organiser for the breast or a genetic abnormal reactivity of the breast tissue to male hormones. The male Seabright bantam has female feathering, and the cause of this abnormality is not that the testis of this male bird produces female hormones but that the feathers respond in an abnormal way to the normal male hormone. This deep constitutional gynecomastia is explained by the Seabright-Bantam syndrome of Fuller Albright.

Hypotestosteronic Gynecomastia. This form is encountered in hypotestosteronic conditions, thus in male eunuchoidism and Babinski-Frohlich disease, and constitutes a part of the general clinical picture. Its production is explained by the unchecked action of male œstrin through deficiency of the antagonistic testosterone.

The gynecomastia seen in certain cirrhoses of the liver is also explained by the hyperœstrinic mechanism. Here the male œstrin is not neutralised normally by the liver on account of the liver deficiency.

Hypertestosteronic Gynecomastia. Selye has shown experi-

mentally that testosterone as well as œstrin can stimulate breast development, a fact demonstrated clinically by the occurrence of gynecomastia in patients undergoing testosterone treatment. The gynecomastia seen in teratomas of the testis and tumours of the interstitial cells of the testis probably belongs to the group of hypertestosteronic gynecomastia. I say "probably" because it is possible that these testicular tumours secrete œstrin and not testosterone. At all events the possibility of hypertestosteronic gynecomastia should impose caution in using testosterone for the treatment of all gynecomastias.

Cortilactinic and Prolactinic Gynecomastia. These are determined by an excess of adrenocortical cortilactin or antepituitary prolactin (or, to use a better term, ante-pituitary mammogenin). These hormones stimulate the breast and determine a gynecomastia either of glandular or of complete lactating type. Thus the cases of "lactation in the male" described with so much exaggeration in the older literature belong to cortilactinic or prolactinic gynecomastia. Cortilactinic gynecomastia is encountered in some adrenocortical tumours of the male. Prolactinic gynecomastia is seen in some cases of eosinophile adenoma. They are very rare and form part of the general clinical picture of these tumours.

Therapeutics of Gynecomastia. Except for the gynecomastia encountered in cirrhosis of the liver, in which treatment of the cirrhosis is the primary concern, the gynecomastia secondary to an adrenocortical or a pituitary tumour, where treatment centres on the causal condition, and the gynecomastia due to cortin or testosterone administration, surgery is the only treatment of this condition. It is indicated not only for deep constitutional but also for hypotestosteronic forms, because even in the latter endocrinotherapy, for an unknown reason, gives no results.

Happily, surgeons have evolved remarkable techniques for plastic reconstruction of the human breast.

CHAPTER VII

THE MALE HERMAPHRODITISMS

(GENITAL ANDROGYNOIDISM, GONADAL ANDROGYNOIDISM)

THE term hermaphroditism, in the present state of science, is applied to a constitutional disease characterised by a severe intersexualisation affecting the genital organs and tract and the gonads. According to the genetic sex of the hermaphrodite a male and a female hermaphroditism are described. According to the degree of intersexualisation a genital and a gonadal hermaphroditism are distinguished.

This is the definition embodying the contemporary conceptions. Before reaching this conception, however, the natural history of hermaphroditism passed through various phases.

Hermaphroditism was first described—if the term description can be applied to the naive repetition of fairy tales—by Pliny, who limited this human condition to the dæmonological speculations of the ancient Eastern peoples on the existence of bisexual beings. In fact, hermaphroditism originally meant bisexuality. Pliny's lead was followed by many Renaissance physicians such as Paolo Zacchia, Jacques Duval, Johannes Wier and Ambroise Paré.

A glimpse of light appeared in the legislative work of Ulpianus in the second century, with his conception of the predominant sex of the hermaphrodite. This was developed by Ambroise Paré, who wrote of male and female hermaphrodites but, adhering to the dæmonological conception of bisexuality, he added a third group of bisexual or complete hermaphrodites and a fourth group of neuter hermaphrodites.

In the nineteenth century Klebs, summarising the work of that period, described with greater precision the male and female hermaphrodites of Ambroise Paré as male and female pseudo-hermaphrodites. He maintained the existence of the bisexual or complete hermaphrodite, which he described as "true hermaphrodite." Ambroise Paré's neuter hermaphrodite is perpetuated even in recent text-books as individuals of "undetermined sex."

To-day, recent biological work shows hermaphroditism to be

PLATE V



7. Male genital intersex, hypospadiac form (a case of Young)

hermaphroditism are described. According to the intersexualisation a genital and a gonadic type are distinguished. The conception of hermaphroditism embodying the contemporary conception of intersexualisation, however, the natural history of hermaphroditism has passed through various phases. The term was first described—if the term descriptive is not to the naïve repetition of fairy tales—by Plinius, who attributed human condition to the dæmonological speculation of ancient Eastern peoples on the existence of bisexual hermaphroditism originally meant bisexuality. This view was followed by many Renaissance physicians such as Jacques Duval, Johannes Wier and Ambroise Paré.

Light appeared in the legislative work of Ulpian in the 3rd century, with his conception of the predominant hermaphrodite. This was developed by Ambroise Paré into a type of male and female hermaphrodites but he maintained the dæmonological conception of bisexuality, his group of bisexual or complete hermaphrodites and of neuter hermaphrodites.

In the 19th century Klebs, summarising the work of Ambroise Paré, described with greater precision the male and female hermaphrodites of Ambroise Paré as male and female hermaphrodites. He maintained the existence of the complete hermaphrodite, which he described as a "neuter hermaphrodite." Ambroise Paré's neuter hermaphrodite is even in recent text-books as individuals of

8. Male genital intersex, hypospadiac form (a case of Young)

[To face p. 53.]

Many may become fixed throughout life, but sometimes the feminine features retrocede spontaneously. This happens in androgynoidism with cryptorchidism, when the testis descends into the scrotum and is placed thus in condition for more active secretion of masculinising hormones. It was this event that was described by Roman and Renaissance physicians as change of sex, "always from female to male." The remasculinisation bears principally on morphological and psychological characters. To such an occurrence Ambroise Paré referred in his story of Germaine Marie, a "girl" who at the age of fifteen leapt over a stream while running after her pigs and to "her" horror saw male genitals. And Montaigne adds that a song became current in the region warning girls against jumping too high. A much more precise observation comes from Raoul Blondel. It was the case of a married "woman," whose marital life was happy although she knew that she could never have children because she had never menstruated. Intercourse was possible but difficult because her vagina was small (3 cm.) and during intercourse she had erections of the clitoris (in fact a hypospadiac penis) and ejaculation. Libido was of distinctly female type. At the age of forty-five "she" fell from a height of 13 feet, after which accident two "glands" descended into the labia majora, and these were demonstrated as testes with epididymis and vasa deferentia.

DEEP CONSTITUTIONAL MALE GONADAL HERMAPHRODITISM (GONADAL ANDROGYNOIDISM)

The clinical history of genital androgynoidism is based on cases in which feminisation of morphological, psychological and genital features coincides with the existence of gonads of male type, this gonadal feature weighing so heavily in the balance of sexual characters that these individuals are considered genetically male. The clinical history of gonadal androgynoidism is based on cases in which feminisation bears on morphological, psychological, genital and gonadal features. As the gonads are mixed male and female it is not possible to state whether these individuals are genetic males feminised to such a degree as to show also ovarian elements or genetic females masculinised to such a degree as to show testicular elements. In other words, anatomoclinically it is impossible to know whether the hermaphroditism

is male or female. The only way out of this difficulty (as we have seen that real bisexuality cannot exist) is to take the will to sex as basis, and to consider as male gonadal androgynoids those severe intersexes who possess testis and ovary but will to be male. It is thus according to the pragmatic sex that this form is isolated and described.

The general clinical picture resembles that described for the preceding form, male genital hermaphroditism. There is the same mixture of male and female morphological and psychological features, the will to the male sex predominating among the latter. The external genitals and genital tract show a similar mixture of male and female features, with a certain male predominance as described for the genital form. The sexual functions, libido and potency, show also various degrees of maldevelopment and feminisation described in the preceding form. Here also, for anatomical reasons intercourse can take place in both male and female modes, but gonadal male hermaphrodites experience greater pleasure in intercourse with women.

The essential characteristic, however, is the mixture of male and female features in the gonads, because the gonads of these genetic males have undergone a feminising process. The feminisation of the gonads is of varying degree, and once more anatomoclinical observations repeat biological experiments. In mild forms the ovary, whether independent or connected with the testis as ovotestis, is very rudimentary and the testis better developed. In severe forms a well-developed and functioning ovary exists side by side with a functioning testis (case of Urecchia and Teposu). In other cases an undeveloped testis coincides with an undeveloped ovary, recalling the biological experiments of heterosexual symbiosis or grafts in which both heterosexual gonads are of equal potency and inhibit mutually their further development. Whether humans can show feminisation of both testes (males with two ovaries and no testis) as occurs in experimental biology is not known. The presence of ovary and uterus in such male intersexes can give rise to menstruation.

Male gonadal hermaphrodites can show unilaterality. In such cases ovary and female genital formations can exist on one side of the body, testis and male genital formations on the opposite side. Such cases approach the intersexual birds described by zoologists as gynandromorphs.

The course of the disease is similar to that of the preceding

form. On the whole they seem better adapted mentally, and neither very severe psychoses nor suicide have been reported.

Illustrative Case of Male Genital Hermaphrodite of Hypospadic Form

The following case (Hugh Hampton Young, "Genital Abnormalities," p. 52) illustrates this form of intersexuality. This patient, on account of the anomalous state of the genito-urinary organs, was regarded first as a female, was reared as such and attended a girls' boarding school. Doubts about his sex occurred a few months before admission because the voice deepened, erections of the clitoris occurred and he had sexual intercourse with girls at the school.

PROTOSEXUAL (MALE)

Testes just outside inguinal canal. No spermatozoa.
Epididymis both sides, penis short, held back by congenital chordae.
Prostate and seminal vesicles, but undeveloped.
Libido towards women.
General male appearance. Hair of male distribution.
Male psychology.

INTERSEXUAL (FEMALE)

Urethra of female type opening in mid-perineum (hypospadias, penneal type).
Labia minora (on each side of urethra folds suggesting labia minora).

Illustrative Case of Male Genital Hermaphrodite (H. H. Young, "Genital Abnormalities," p. 84)

PROTOSEXUAL (MALE)

Testis on left (no spermatogenesis but interstitial cells abundant).
Vas left, penis, prostate.
Male habitus except for hair.
Male psychology and will to be male.

INTERSEXUAL (FEMALE)

Labia majora, hypospadias, vagina, uterus (at 15 $1\frac{1}{2}$ cm. wide, 1 cm. thick), tubes.
Hair of female distribution, female pubescence.

The history of this patient is of great interest. He had been brought up as a boy in an orphanage. At the age of seven, following an operation and the discovery of vagina and tubes and of a gland resembling an ovary, he was considered female and his name changed from Frank to Frances. Later, the penis (taken for a hypertrophied clitoris) was removed because of masturbation.

At the age of sixteen a testis was discovered at operation on the left side, with vas. It was excised. The patient was still under the jurisdiction of an institution for girls, but declared that as soon as "she" became of age she would assume male attire. In

fact "she" did become male and is employed as a truck driver, apparently happy although living as a male without a penis or testicles but with a vagina.

Cases like this teach us that it is imperative to defer sex-formative operations until the age of sex consciousness, and that the will to sex is the most important factor and can correct imperfect objective interpretations.

This case represents a unilateral intersexuality. Testis, epididymis and vas deferens were all on the right side, while the ovary was on the left.

On the basis of the will of the patient, and notwithstanding hesitation on objective grounds, uterus and ovary were removed. The patient felt much better in consequence.

A case of Ombrédanne (Case XXIV in "Les Hermaphrodites et la Chirurgie," p. 299) is similar except that both tubes were present and satisfactory intercourse with females occurred.

Balance Sheet of Sexual Characters in a Case of Male Gonadal Hermaphroditism (Lindvall-Wallgren's case, Virchows Archiv. 297, 1, 1936).

PROTOSEXUAL (MALE)	INTERSEXUAL (FEMALE)
Testis in right half of scrotum. Microscopically incomplete spermatogenesis.	Left ovary. All grades of development of follicles including corpus luteum.
Right scrotum with testis, epididymis, vas deferens. Penis (hypospadiac urethra).	Menstruation. Blood in urine every month for 2 or 3 days since the age of 15.
General appearance male, muscular and straight (except for width of pelvis and hair distribution).	Uterus normal for age of patient, near the left side. Tube on left side. No prostate or seminal vesicles. Hypospadiac urethra. Breasts of female type, increasing in volume before menstruation.
Adam's apple developed.	Pelvis wide female type. Hair of female distribution (no hair on face or body, transverse pubescence).
Strong libido towards women. At the time of observation engaged to be married. Will to be a male expressed to the surgeon. Deeply distressed because rejected for military service.	Female voice.

The Case of Karl Hohmann. Karl Hohmann was studied intensively by Friedreich in his Heidelberg clinic, then by Bernhard Schultze in his clinic at Jena, then by v. Kolliker and v. Recklinghausen in Wurzburg, Krause in Budapest, Hoffmann in Bale, and others. Hohmann's claim to be regarded as a *male intersex* is based on his will to maleness. Although well studied,

this case is incomplete because of the lack of anatomical exploration, but it is quoted here because of its historical significance.

Hohmann was a male (will to maleness, male fertility, but possessed strongly feminine features, gonadal and genital (intercourse of female type) and morphological. His biotypological diagram has been drawn up as follows:—

PROTOSEXUAL (MALE)

Testis right Living spermatozoa in ejaculate. Male fertility (a son).

Right scrotum (containing testis). Left scrotum empty. Penis Erections and pollutions at 15. Intercourse with women (more enjoyable than with men)

Pelvis of male type. Right side of body (testis side) more developed than left (probable ovary side). Male character and will.

INTERSEXUAL 'FEMALE'

Ovary found only on palpation. Menstruation. Blood issued from sinus urogenitalis Onset at twentieth year, 3-4 week cycle, then more irregularly until complete cessation at 47.

Urethra of female type. Perineal opening in sinus urogenitalis, where vagina also opened. Uterus rudimentary and tubes on clinical exploration. Mammaræ of female type retroceding at menopause. Intercourse with men possible by the conformation of the external genitals but less enjoyable than with women.

General appearance female except for pelvis. Hair female distribution

CHAPTER VIII

VIRILISM

(MORPHO-PSYCHOLOGICAL GYNANDROIDISM)

FEMALE intersexes, *i.e.*, individuals whose basic genetic sex is female but in whom the interplay of a deficient genetic-organiser-endocrine feminising impulse and of an abnormal reactivity of the body cells has made for abnormal female sexual differentiation, are here described, as were their male counterparts, in groups constituting special nosographical categories according to the degree of intersexuality.

Virilism represents the first degree of female intersexuality. Masculinisation bears on the morphological and up to a certain point on the psychological features, the genital and gonadal features remaining distinctly female.

This condition was first described by Hippocrates in the fifth century B.C. The physiopathological mechanism was elucidated much later. The connection between a disturbance of the adrenal glands and virilism, and thus the establishment of the particular form of adrenal virilism, dates from the memoir of Bulloch and Sequeira (1905) and principally from the work of L. R. Broster and his Charing Cross co-workers since 1931. The connection between another class of virilism and an ovarian masculinising tumour, and thus the establishment of the physiopathological form ovarian arrhenoblastoma virilism, dates from the work of Robert Meyer from 1915 onwards. The conception of a deep constitutional virilism depending on sex reversal in the pre-endocrine phase of embryonic life results from the recent work of embryologists and geneticists. Thus according to the predominant physiopathological mechanism involved various forms can be described.

ADRENAL VIRILISM

This is an endocrine virilism physiopathologically based on hypersecretion of the adrenocortical masculinising hormones, which are of steroid nature and can be described by the general term "corticogenitalin." This hypersecretion can originate in an adrenocortical hypersecreting tumour (adrenal hypercorticogenitalism). It may be due to a primary hypersecretion of adrenotropic hormone from the pituitary, causing

PLATE VII



11. Two female morphological intersexes (the lower figure is the photograph of a well-known German woman rider), from the collection of Magnus Hirschfeld.

adrenocortical hyperfunction and thus determining a pituitary-adrenal virilism. Such is the virilism arising from hypersecretion of adrenotropic hormone from a basophile adenoma (true Cushing's disease). Lastly, it may be due to an abnormal hypersthenic impulse originating in the hypothalamic centre of the corticogenitalin system, transmitted to the ante-pituitary cells secreting adrenotropic hormone and thus causing hypersecretion of this hormone, which in its turn causes hypersecretion of corticogenitalin. In these last cases the intense hypothalamic drive on the antepituitary is manifested by basophile hyperplasia and a special hyalinisation of the basophile cells (Crooke's lesion), and the over-stimulation of the adrenal cortex by adrenotropic hormone is manifested by adrenocortical hyperplasia. This last physiopathological mechanism of adrenal virilism can be described as cerebro-pituitary hypercorticogenitalism. Conditions of cellular reactivity intervene also in this pathogenesis of adrenal virilism.

Primary adrenal virilism is due to an adrenocortical hypersecreting tumour. Pituitary-adrenal virilism is determined by a basophile adenoma of the antepituitary. Cerebro-pituitary-adrenal virilism is due to an interplay of constitutional genetic abnormal liability of the corticogenitalin system and of environmental factors affecting the hypothalamic centre of this system.

Little is known of these environmental factors, but recent work has demonstrated the rôle of encephalitic localisations and of ovarian disturbances (*e.g.*, pregnancy and menopause), which drive the corticogenitalin system into abnormal compensatory reaction.

The Common Form. The morphological features, the habitus, are the essential clinical characteristics. These features and the voice approach masculinity in most cases. The face is expressive, often hard, and has not the flowing lines and smoothness of femininity. Its skin is hard and often thick with acne, and hair is more or less developed as beard and moustache. The body shows distinct muscular relief as in the male, for the muscles are well developed and lack any great fatty covering. The shoulders appear strong and are wide in proportion to the pelvis, which also is of male type. The undeveloped mammae contribute to the masculine impression. The limbs are straight and do not form the female genu valgum. Hair grows on body and limbs, and the pubescence is triangular. The gait is energetic.

The sexual system is distinctly female. The gonads are female. The genital organs and tract also are distinctly female except for hypertrophy of the clitoris, which thus tends to become a penis in some cases. However, a certain hypoplasia of vagina, uterus and ovaries is often described, and is due to the female-inhibiting action of the masculinising process, *i.e.*, of corticogenitalin. Sexual functions vary. Menstruation exists, although often scanty and irregular. Fertility also exists but is often below par. Frigidity is very frequent. Libido varies. In many cases it is deficient because of endocrine inhibition through the masculinising hormone but also because of psychological factors. In other cases it exists and is of female type, and such women may lead a happy marital life. In the most characteristic cases, however, libido is of male type and results in female homosexuality. Psychogenic factors play an important rôle in the libido manifestations, which are of great clinical importance, the source of many conflicts and manifested by various symptoms masking the sexual conflict.

The general psychology varies, but usually shows male tendencies. Such women are dominating, inclined to outward activities and sports, which are promoted by the usually notable development of their muscularity. The general psychological picture is complicated by various behaviour disturbances due to an abnormal reaction of the psyche to the disease, and by psychoses due to various factors acting on these constitutionally inferior individuals.

The biochemical syndrome is important. The various metabolisms have not as yet been thoroughly studied. Their disturbance indicates involvement of the metabolic regulatory function of the adrenal cortex or a coincident involvement of other metabolic factors of the antepituitary. Thus in some cases increase of basal metabolism, increase of non-protein nitrogen in the blood, hyperglycæmia and a slight decrease of blood chlorides are encountered. The hormonal findings are much more significant. The 17-ketosteroids are increased in the urine especially in neoplastic cases—a finding that may help in the diagnosis. The presence of free male hormone (Patterson and Green) in the urinary androgens is an important finding. Urinary oestrogens also are increased, particularly in adrenal neoplastic cases. The androgen-oestrogen ratio is reversed, androgens being relatively much more abundant in the urine of these patients than in that of

PLATE VIII



12. Female transvestist pictures of the French animal painter, Rosa Bonheur.

normal women. Pregnanediol glycuronate also is increased in the urine.

This disease is essentially chronic and does not retrocede spontaneously. Cases due to an adrenocortical tumour depend on the course of the tumour, and thus improve after removal of the tumour and relapse with cachexia when the tumour, if malignant, reappears and causes metastases. Pituitary-adrenal virilism also depends on the course of the causal basophile adenoma, but mild cases usually improve with oestrogens. Cerebro-pituitary adrenal virilism may retrocede with oestrogens in mild cases, severe cases yielding to adrenalectomy as performed by L. R. Broster

Special Forms. *The Amazonian form* is very frequent but may be of deep constitutional as well as of adrenal origin. It is a mild form of virilism, lacking the repellant aspect of the complete form and, on the contrary, displaying a certain elegance. These are women excelling in sports and other male activities, and exhibiting qualities of leadership. Their physique is mildly but elegantly masculinised, the expression of the face definite and energetic, the body muscular and resilient, the gait steady. There is a certain tendency to homosexuality, usually manifested by incompatibility in marriage. Such women are often admired both physically and mentally, although, as a visitor to the historical Amazon Lady Hester Stanhope wrote, "They do not arouse tender sentiments."

Hirsutism is a special form of adrenal virilism, characterised mainly by the development of hair on the face and body, thus by an exaggeration of male hair distribution.

Cushing's disease results from hyperfunction of many hormonal systems—the corticogenitalin system, the diabetogenin system (antepituitary diabetogenic hormone), and others. The hypersecretion of these hormones may originate in the abnormal hypothalamic impulse transmitted to the antepituitary, in a basophile adenoma of the antepituitary and, in rarer cases, in an adrenocortical tumour. The clinical picture of virilism is only a part of the general clinical picture. Concomitant manifestations are a particular obesity of male type (trunk and face), hypertension, diabetes (Achard and Thiers' *diabète des femmes à barbe*), osteoporosis leading to cyphosis.

Female pubertas præcox with virilism is a combination of precocious somatic and sexual development with virilism. It is

due to hyperfunction of the adrenal genital cortex (neoplastic or primary adrenal or cerebro-pituitary adrenal) occurring after birth and before the age of puberty.

Menopausal virilism is a special form representing an abnormal compensatory reaction of the corticogenitalin system to involutional hypo-ovarism. The mother-in-law of the music-halls is a caricature of this form. Under the influence of this reactive hypercorticogenitalism at menopause such women grow hair on the face, which acquires a hard and virile look. Their voice becomes rough and their temperament domineering and masculine.

Psychological forms corresponding to those described for male feminism are frequent. Female homosexuality and female transvestism are outstanding. Striking examples of the latter form are George Sand and Christina of Sweden. Joan of Arc does not enter into this category. In my opinion she was essentially a mystic, and her transvestism originated in her mystical temperament and not in any intersexual element.

ARRHENOBLASTOMATOUS VIRILISM.

This is an endocrine virilism and is determined by an ovarian tumour composed of cells secreting an excess of androgen. These masculinising ovarian tumours, known as arrhenoblastomas, probably develop from testicular rests or aberrant adrenocortical cells in the ovary. The clinical picture is similar to that of the complete form of adrenal virilism, except for the presence of an ovarian tumour. I have not encountered any *formes frustes* of this condition. The biochemical syndrome has not been studied to any extent, and differences from that of adrenal virilism are not yet known. Abarbanel found in his case a high quantity of androgens in the urine and an increased creatine retention.

DEEP CONSTITUTIONAL VIRILISM

In this physiopathological form of virilism the constitutional regulator disturbed is essentially the genetic regulator. An abnormal gene causes metabolic dysfunction in certain cells, particularly in those constituting the sexual formations, so that their reactivity to sexual hormones is modified. They react even to feminising hormones by developing towards masculinity, or alternatively they become more sensitive to the masculinising hormones which are normally present in the female. This genetic

reactivity factor exists in all virilisms. When it is preponderant the condition is a genetic virilism. Its etiology is that of gene mutation in general.

Clinically deep constitutional virilism may show any of the forms described with adrenal virilism, but usually it manifests itself in the Amazonian form or a special hypertrichotic form. The latter is characterised by an intense body hypertrichosis, either generalised or localised on the lower limbs or abdomen. The intensity and localisation of the hypertrichosis, combined with the absence of other features of masculinisation and the regularity of menstruation, give to these deep constitutional cases a special stamp.

Therapeutics of Virilism

The object of treatment of virilism is re-feminisation. In other words, we strive to perfect the genetic sex of the individual.

Primary adrenal virilism which is due to an adrenocortical tumour must be treated surgically. Pituitary-adrenal virilism (virilism from basophile adenoma) must be treated with oestrogenic hormones, which often give brilliant results, and by irradiation of the pituitary. These procedures must be completed by psychotherapeutic, physiotherapeutic and general constitutional measures. Cerebro-pituitary virilism must be treated with oestrogenic hormones combined with psychotherapy and general constitutional methods. In advanced cases partial adrenalectomy, as performed by L. R. Broster, gives excellent results.

As it is difficult to distinguish these three varieties of adrenal virilism, it is practical (except when an adrenal tumour can be diagnosed clinically or radiologically, or indicated by a very highly abnormal quantity of androgens in the urine) to begin with oestrogenic hormones. Like all other forms of endocrinotherapy, this method is delicate and highly specialised. In skilled hands and with collaboration from the subject (who requires patience and tenacity to follow this lengthy treatment) results are often excellent, although miracles cannot always be expected. If hormonotherapy and pituitary irradiation fail, patients should be surgically explored and treated in consequence.

Hypertrichosis causes the most rending anxiety to such patients. Local treatment with oestrogen ointment has given me excellent results. Electrolysis and other depilatory measures are not without danger, but there is room for development of such local

procedures. Their application is in the domain of the dermatologist.

Deep constitutional virilism is treated with the hormonal and psychotherapeutic measures indicated for cerebro-pituitary adrenal virilism. Results are of course less definite but sufficient to warrant persisting with these methods. Local methods of depilation are here particularly indicated, and should be used by a dermatologist.

Ovarian virilism is treated by removal of the tumour.

CHAPTER IX

THE FEMALE HERMAPHRODITISMS

(GENITAL GYNANDROIDISM AND GONADAL GYNANDROIDISM)

LIKE its male counterpart, female genital hermaphroditism represents a higher degree of intersexualisation (here, of masculinisation), the intersexualising process having involved the external genitals and genital tract. The gonads remain distinctly female. This condition corresponds to the female pseudo-hermaphroditism of Klebs.

Adrenal Female Genital Hermaphroditism (Adrenal Genital Gynandroidism). This is a genital gynandroidism determined by hyperfunction of the adrenal "genital" cortex occurring in embryonic life. As already delineated, such an adrenocortical hyperfunction occurring after birth gives rise not to an adrenal female genital hermaphroditism (genital gynandroidism) but to a virilism. This hypersecretion of the adrenocortical androgens may be due to a hypersecreting adrenocortical tumour (primary adrenal female genital gynandroidism) or to an intensive drive of the diencephalic centre for cortigenitalin, in which case hyperplasia of the adrenal cortex is encountered (cerebro-pituitary adrenal genital gynandroidism).

The *gonadal characters* are of female type. Ovaries only are encountered, and not testes. However, here also the ovaries are below par through inhibition exercised by the masculinising process; hence infertility, hypomenorrhœa and amenorrhœa.

The *genitals* show various degrees of masculinisation. The clitoris is hypertrophied to the extent of acquiring the dimensions and form of a penis, often complete with glans (moderate hypertrophy of the clitoris is a racial characteristic of certain primitive peoples). The urethra is masculinised. In some exceptional cases cited by Ombrédanne it is completely masculinised and thus takes the form of a closed canal opening with a meatus at the glans of the clitoris-penis. In general, however, masculinisation does not attain such a degree; the urethra remains an open groove and follows the inferior surface of the penis-clitoris, giving a picture of female hypospadias. In many other cases it remains of female type and opens in mid-perineum.

The labia minora retain the female features except in rare cases, when they constitute urethral folds on each side of a hypospadiac urethra or even unite to close the urethral groove, thus forming a male type of urethra. The labia majora also retain female features except in some very rare instances in which they join and form a scrotum. Vagina, tubes, uterus exist as in normal females except that they may be undeveloped owing to the masculinising process. The rest of the genital tract does not undergo masculinising change. Prostate has been observed, but its significance has been debated. Epididymis and vas deferens have never been noted in female genital intersexes.

By virtue of the special morphology of the genital organs such individuals can act sexually both as male and as female. The clitoris-penis undergoes erection but gives no ejaculation, and notwithstanding its relative smallness and the hypospadias can penetrate a female vagina.

Morphologically such patients have either a predominantly male or predominantly female habitus. The latter is more frequent, but the former combined with the male appearance of the genitals has given rise to many errors of sex. Andromasty in particular is a constant feature.

Psychologically also these patients show predominantly male or predominantly female features. Libido is usually of female type, but instances of male type have often been reported, and a few female genital intersexes have even married as men. Although ambivalent intercourse is possible, ambivalent libido, although possible theoretically, has not been noted in genuine observations of female genital intersexes. The will is either to maleness or to femaleness, the pragmatic thus failing to correspond to the genetic sex in the latter case.

Contrary to their male counterparts, female genital intersexes are usually of exclusively endocrine origin and result either from hyperfunction of the adrenal cortex, in most cases through a tumour, or from a virilising tumour of the ovary. The intersexual state retrocedes with endocrine surgery directed to these factors, and up to a certain point after intensive therapy with oestrogenic hormones.

This clinical history is based on demonstrated female genital intersexes (*i.e.*, intersexes possessing ovaries but no testis). In a nosographical description no account can be taken of all the gynandroids or female pseudo-hermaphrodites described in the

PLATE IX



123. Female genital intersex: a case of Neugebauer.

literature but without adequate investigation and thus without absolute determination that ovaries are present and testes absent. Many of these imperfectly studied gynandroids may have been male intersexes, male pseudo-hermaphrodites or gonadal intersexes male or female.

In adrenal neoplastic cases the course depends on the neoplasm. In cases with adrenal hyperplasia (cerebro-pituitary adrenal genital gynandroidism) the disease becomes arrested, and there are cases of such individuals living and marrying as males. Behaviour disturbances, psychoneurotic complications and psychoses determined by the maladaptation and the conflict complicate the course of the disease.

Deep Constitutional Female Genital Hermaphroditism (Deep Constitutional Genital Gynandroidism). In opposition to male genital hermaphroditism, which is always deep constitutional and never endocrine, female genital hermaphroditism is most frequently endocrine adrenal.

The deep constitutional cases show clinically a picture similar to that of hyperplastic adrenal genital hermaphroditism (cerebro-pituitary adrenal genital gynandroidism). They are, however, often more fixed, better adapted and usually less accentuated.

Deep Constitutional Female Gonadal Hermaphroditism (Deep Constitutional Gonadal Gynandroidism). Gonadal gynandroidism, which is always deep constitutional, represents the highest degree of female intersexuality, the masculinising process involving the gonads themselves. Like its male counterpart it is always deep constitutional.

Genetic females can be experimentally intersexualised up to the extent of partial masculinisation of their gonads. In this manner are produced female intersexes possessing ovaries and testis. As already said, however, in connection with male intersexes, it cannot be demonstrated absolutely that individuals possessing ovary and testis are genetic females masculinised or genetic males feminised. The balance of sexual characters is not clear and thus description of individuals possessing testis and ovary as female gonadal intersexes is based on their will, i.e., on the pragmatic sex.

- The clinical picture resembles that of male gonadal intersexes except for the presence of more important female morphological features and the will to femaleness.

The gonadal features are a mixture of maleness and femaleness

in various proportions. In extreme cases separate ovaries and testes are seen. In moderate cases the gonad or gonads are formed of ovarian and testicular tissue (ovotestis). In extreme cases, as in that described by E. Witschi and W. F. Mengert, the gonads appear as testes, but their structure is peculiar in that follicles like vesicles are found in the testicular tissue. In cases in which hormones have been investigated there is predominance of oestrogens. Menstruation may be disturbed when the inhibiting masculinising process is intense.

The genital as well as the morphological features also present a mixture of male and female elements.

The psychological features show a definite preponderance of female characteristics. Libido, when it exists, is towards males. There is a will to femaleness.

Therapeutics of Hermaphroditism in General

To avoid repetition the general lines of handling hermaphrodites, whether male or female, genital or gonadal, are here discussed.

The attitude towards male hermaphrodites, *i.e.*, genital and gonadal intersexes, has changed in the course of the centuries. The ancient Eastern peoples regarded severe intersexes with superstition, as expressions of divine will and intervention, an attitude prevailing nowadays among primitive peoples. The Greeks, banishing the supernatural from their consideration of intersexes, adopted towards them a reasonable and humane attitude. The Romans reacted very differently, regarding hermaphrodites as expressions of divine wrath and portents of national calamity and putting them to death to pacify the gods and avert catastrophe. In the later Roman period this cruelty waned because intersexes in general, and mild male intersexes in particular, were in great demand for the imperial orgies. An attempted reversion to the primitive Roman cruelty by Constantine the Great failed as it fell on the Eastern Roman Empire, *i.e.*, on Greek soil. In the second century the Roman jurist Ulpianus introduced more humane laws for these unfortunate beings, giving them civic rights and the prerogatives of the sex held to predominate in them.

The Renaissance saw the re-introduction of the ante-Greek attitude of savage superstition towards hermaphrodites. As late

PLATE X



14 Female genital intersex (Virginia Mauri, described also as
Sefu Alkahissa)

as the sixteenth century Bauhin, the renowned anatomist and professor of Bale University, demanded death for hermaphrodites, whom he held to be signs of divine displeasure. Even when superstition had begun to wane cruelty persisted, and hermaphrodites were put to death when they used the prerogatives of the sex other than that which they had chosen or been forced to adopt. Instances of this procedure have been reported by Bauer, Arnaud and Venette as having occurred in the sixteenth and seventeenth centuries.

Under the influence of Johannes Wier and chiefly of Ambroise Paré a more human attitude prevailed. A humane law introduced by an unknown legislator, completing the legislation of Ulpianus and amplified by Ambroise Paré, allowed hermaphrodites to choose their sex, although it provided severe punishment for those who did not adhere to the chosen sex. This last remnant of cruelty towards hermaphrodites disappeared gradually with the growth of enlightenment, and to-day hermaphrodites are considered as sick people to be approached with sympathy and understanding and treated with all the resources of the art of medicine.

Registration and Education of Intersexes. The sex of mild genital intersexes can often be determined accurately at birth by a skilled physician, but difficulty arises for severe genital and gonadal intersexes. Here the genetic sex cannot be discovered with certainty, the pragmatic sex obviously cannot be determined at so early a stage of life, but nevertheless these individuals have to be registered and reared either as males or as females. For such cases Charles Debierre has proposed registration as "undetermined sex," and a more exact determination later, at puberty. However, even in childhood the lack of sexual determination is a great handicap and may have serious consequences later in life.

For practical reasons these severe genital and gonadal intersexes, individuals of doubtful sex, are registered at birth as males. This is justified by the fact that most of these individuals are indeed genetic males, and by considerations of education. It is a fact that a female hermaphrodite in a girls' school is a source of much less mischief than a male hermaphrodite, who can act sexually as a male and thus deflower "her" schoolfellows. A female hermaphrodite in a boys' school can, theoretically, be violated, but practically speaking this never happens as these

individuals do not attract attention through their abnormality; their large clitoris passes for a penis, and their vagina, particularly before puberty, is totally undeveloped and masked by incomplete union of the labia. It is obvious that physicians should exercise great care in advising on the registration of intersexes.

Treatment of Hermaphrodites. In hermaphroditism in general the object of treatment is to perfect the sex willed by the patient, *i.e.*, the pragmatic sex. It is cruel to force such individuals into a sex they do not will, even if that sex is the genetically and thus absolutely true one. Such a procedure is catastrophic, whereas respect for the will to sex of these unfortunate hermaphrodites helps them to better adaptation and happiness. Because of this principle definite sex-formative operations should not be undertaken in severe intersexes at an early age, *i.e.*, before the dawn of sex consciousness. Many patients have not thanked their surgeons for having rashly given them a sex which they rejected on reaching maturity. Even such apparently simple interventions as correction of a hypertrophic clitoris should be postponed in many cases until after puberty, and in general sexual plastics for children should be considered with the strictest regard for individualisation.

The principle of respect for the will of the patient offers difficulties in cases of female intersexes of adrenal origin, who are distinctly genetic females, sex reversal having occurred late, *i.e.*, at the endocrine stage. Here operation during infancy should not be deferred. In the first place, most of these cases are due to tumours which usually evolve malignantly, and the neoplastic indication predominates over that of intersexuality. Furthermore, even if a tumour is not found at operation—and the absence of tumour cannot be ascertained before operation—but only adrenocortical hyperplasia, adrenalectomy should be performed because results, as shown by the work of L. R. Broster, are so definite and so striking that it is our duty to prepare such patients for the joys of perfect womanhood instead of condemning them to linger in the miseries of intersexuality.

For adult cases, however, the problem is slightly different. In general female adrenal intersexes strive towards womanhood, and the question is thereby simplified. Some, however, as in the original observation of Crecchio, will be males. Two of Fibiger's patients were even happily married as "men." For

these the will must be respected when there is no evidence of malignant tumour, the possibility of which can be eliminated when the condition shows long and chronic development. Thus the principle of the pragmatic sex must be followed. otherwise these patients are faced by despair and misery.

Sexual Plastic Surgery or Sexual Orthopædics has recently made gigantic strides, as witness the cases published by Lagos Garcia, Hugh Hampton Young and L. Ombrédanne. It makes even a thoroughgoing internist yearn towards surgery when he reads how the surgeon-sculptor can make of unfortunate hermaphrodites well-formed males and females. Not only perfected technique but also biological principles have made these marvels possible. In truth these reports impress on the reader that biological principles, so slowly penetrating into internal medicine, have been assimilated with great rapidity by surgeons. Is it because the biological spirit was introduced into the healing art by a surgeon, John Hunter?

Sexual orthopædics has developed principally only of recent years. The operation proposed for gynecomasty and probably applied by Paulos of Ægina was the first procedure of this sort, but more radical sex-formative interventions were not performed until the end of the nineteenth century, not only because of difficulties of technique but principally because the surgeons of old were averse to touching the intersex, fearing to interfere with divine providence. Albertus Magnus reported probably one of the first sexoplastic interventions, consisting in section of a "membrane" which allowed male organs to appear. He added, however, that this did not amount to conferring a particular sex on the patient, but merely allowed the real sex to appear, and was thus not an act against God. In the sixteenth century Realdus Columbus refused to rid an unhappy Ethiopian woman of a hypertrophic clitoris which prevented her from having any intercourse and made her life miserable. He was reluctant to assume responsibility, and the same hesitation is reflected in the work of the eighteenth century surgeon Arnaud.

When more liberal views prevailed, and particularly when the will of the patient was taken as guide, this hesitation vanished, and the operations described in the works quoted can be regarded as some of the finest achievements of modern surgery.

Surgical Endocrinotherapy in Severe Intersexes. Removal of an adrenocortical masculinising tumour, adrenalectomy and removal

of an ovarian masculinising tumour have the same indications as in extra-genital intersexes.

Removal of the gonads demands individual consideration for each case. Haphazard removal, as practised by certain surgeons, is useless vandalism and makes castrates of these patients. In some cases when the genital or gonadal intersex wills to be a male an existent ovary may be removed, and a similar removal of testis may be considered for those who choose the female sex. The effect of orchidectomy, however, is problematic, for the testes of these male intersexes secrete great quantities of œstrin. An observation of Ombrédanne is interesting in this connection. Confronted by an intersex with predominantly female features and the desire to be a woman, this surgeon removed a testis. Severe "menopausal" symptoms followed, unrelieved by testosterone propionate but improved by œstrogens. Close collaboration between internist and surgeon is essential to the success of operative interventions on intersexes.

Constitutional Methods in Genital Intersexes. The predominance of surgery in treatment of these intersexes does not indicate that it is the only method. Here also internistic constitutional procedures are necessary as pre-operative measures and for post-operative adaptation. In this way they enhance the surgical results.

Psychotherapy seems the most important means of effecting guidance and adaptation of intersexes before and after operation. Endocrinotherapy is often useful in deepening the masculinisation or feminisation hewn by the surgeon. The internist, more fully trained in what Sir William Gull called the "general view," has a definite part even in the treatment of genital intersexes. In our days there are no longer specialists in diseases, but specialists in points of view. Severe intersexual diseases must be considered from the point of view of the internist as well as from that of the surgeon, from the point of view of constitutional medicine as well as from that of sexual plastic surgery.

Illustrative Sexual Balance Sheets of Female Hermaphrodites

The Case of Virginia Mauri. This intersex was studied by many Italian clinicians. The most complete report is that of C. Taruffi (*Man. della R. Acad. della Sc. de L'Inst. di Bologna*, 1899, series V, VI, VII, p. 759). Autopsy was performed by Valenti and reported by Pende in his *Endocrinologia*. It showed enormous hypertrophy of the adrenals.

PROTOSEXUAL (FEMALE)	INTERSEXUAL (MALE)
Ovaries. No testes	
Menstruation started at 16	
Labia majora and minora, female type	Penis 5½ cm. long with glans and prepuce.
urethra (hypospadias), vagina, uterus, tubes	
Libido towards men	Libido towards women in early life.
Abortion and one full pregnancy.	Intercourse occurred with women but was painful
	General male appearance.
Pubescence of female type.	Hair of male distribution beard, moustaches) except for pubescence.
	Hair started to grow on face at age of 16 (pubertas præcox)

Schauerte's Case. *Æt.* sixteen, educated as a female, will to femaleness for which the patient asked surgical help.

PROTOSEXUAL	INTERSEXUAL (MALE)
Ovary on left, large, functioning completely with follicles and corpora lutea Menstruation regular from age of 15, every 4 weeks lasting 4 days	Testes right and left Histological examination showed incomplete function
Urethra hypospadiac Labia majora and minora Vagina 8 cm long. Uterus normal size Tubes normal on left, cord-like structure on right Well-developed female breasts	Penis 6.5 cm long Epididymis, vas, cord on the right. Erections at 16.
Pelvis of wide female type Hair female distribution except for upper lip.	Strong muscularity. Hair on upper lip
No libido Will to femaleness.	Rough voice
	No libido. Wild and boisterous.

Case of E. Witschi and W. F. Mengert

PROTOSEXUAL	INTERSEXUAL (MALE)
In the gonads thousands of follicles like vesicles, resembling ovarian follicles (thus microscopic ovaries in ovotestes). Predominant secretion of oestrum	Testes. Small number of germ cells. Spermatozoa present and some rare primary spermatocytes, even abnormal spermatozoa.
Morphological aspect, female	Penis. Bifid scrotum containing testes.
Psychological features female.	
Will to femaleness	

The genetic female sex is accepted by the authors for this individual on the basis of the sex ratio. The pragmatic sex is female.

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